Diagnosis and Treatment of

PERIPHERAL VASCULAR DISORDERS

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For information address PAUL B HOEBER INC
MEDICAL BOOK DEPARTMENT OF HARPER & BROTHERS
49 East 33rd Street New York City 16 N Y

Printed in the United States of America

Library of Congress catalog card number 55 9176

TO MY CHILDREN

JULIE AND BETH

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PREFACE

Only in recent years have peripheral vascular disorders received the study their importance warrants In the past patients suffering from advanced structural alterations in the main arteries in the extremities were considered victims of an incurable malady and the only hope that could be held out to them was that of amputation to control or eliminate the pain of the associated trophic disturbances Few therapeutic measures were available for use in the early cases of arterial insufficiency In fact so little was known in the field that rarely was the diagnosis made before irreversible changes in the form of ulceration and gangrene had occurred As a result the care of such complications fell within the scope of the general surgeon Then it was realized that in certain situations special surgical technics were necessary and hence there evolved a group of vascular surgeons trained in such matters

As interest in the subject increased and extensive research in the physiology of the peripheral circulation was carried out it became apparent that medical procedures too could play a definite role in the field of therapy At present the emphasis is primarily on the early recognition of a *peripheral vascular disorder* at a time when the pathologic alterations are still reversible or when the [illegible]

[illegible] in peripheral circulation

This volume has been written in an attempt to make such knowledge conveniently accessible to the busy family physician by dealing with the various circulatory disorders in such a manner that pertinent information is readily available to him for clinical application After discarding several conventional plans an order of presentation of the material has been evolved which it is hoped will more closely follow the line of reasoning necessary to cope successfully with the problems that arise The contents have been divided into three sections

The first part is devoted to differential diagnosis of those symptoms and signs which indicate the existence of some abnormality of the peripheral blood vessels in the extremities This approach to the subject has been deemed advisable since the physician in his initial contact with the patient is concerned with the problem of interpreting and integrating complaints and physical findings rather than clinical entities Inasmuch as it is essential to possess information concerning the status of the circulation in the extremities for full evaluation of abnormal signs

more comprehensive physiologic viewpoint is desired reference can be made to a companion volume *

It has been felt advisable not to interrupt the continuity of the text by interposing names of workers contributing to the field Instead in most places numbers have been substituted, which refer to a small but selected bibliography at the end of each chapter

Because of the dual presentation of the clinical material i e from the point of view of symptoms and signs as well as of clinical entities and because the physiologic basis for the pathologic changes has been placed in a separate section it has become necessary to make numerous cross references throughout the text Although such a plan may tend to divert the reader s attention from the subject under study it is preferable to the alternative of repetition of the same material in several portions of the book However occasionally this has been done in order to spare the reader from referring too frequently to one section while involved with another

The present monograph is not intended for the specialist in peripheral vascular disorders since such an attempt would have resulted in an unwieldy volume thus defeating the aim of supplying a ready source of reference However if it serves to acquaint the reader with a logical approach to the problem and if at the same time it presents in simple form a clear concept of the diagnosis and treatment of the more common disease entities in this category then its purpose will have been accomplished

* *Vascular Responses in the Extremities of Man in Health and Disease* Chicago Ill University of Chicago Press 1941

several chapters are devoted to a description of those diagnostic tests which can be performed at the bedside or in the office

In the second section of the book are discussed the disorders of the arterial venous, and lymphatic systems, with differential diagnosis being stressed Although a chapter has been assigned to vascular entities affecting other portions of the body, emphasis is on those conditions which involve primarily or solely the vessels of the extremities In most instances presentation of the contents is limited to clinical disorders which are fairly common Numerous accompanying tables deal with a summary of such entities and include as well for the sake of completeness, data regarding conditions which are rare and which probably would not be seen in a general practice

In the second as well as the first section, criteria have been set up to aid in the separation of the patient with a peripheral vascular disorder from the one with a nonvascular entity associated with abnormalities in the limbs Since signs of the latter may also be present elsewhere in the body, in the differential diagnosis it is necessary in every instance to perform a complete physical examination in conjunction with the special tests for circulatory efficiency in the extremities When a vascular and nonvascular condition exist concomitantly, determination of which is largely responsible for the complaints is a difficult problem, an early solution is particularly important in the institution of proper therapy Attempts have been made in the present volume to resolve this issue It is hoped, therefore that with such a clinical approach the subject matter will prove of value to the orthopedist who must differentiate vascular conditions from those due to altered dynamics of the bones of the foot, to the neurologist, who must distinguish ischemic neuritis from diseases chiefly affecting the nerves to the dermatologist who must separate cutaneous manifestations of circulatory disturbances from primary skin disorders and to the chiropodist who must always eliminate the possibility of an impaired circulation to the feet before attempting any local treatment

Therapeutic procedures which are of proven worth or have been shown to possess promise are described in sufficient detail in Section II to serve as the basis for actual treatment without recourse to other sources Proprietary names of drugs have been used, as well as their chemical formulas since it is usually by the trade label that they are known to the medical profession Their source can be found in the appendix Since neither the metric nor the apothecary system has received universal acceptance by the physician in some instances both have been used in indicating dosages of drugs Generally, however such information has been presented in the form of metric equivalents only

The reader will soon become aware of the fact that the medical approach to therapy has been given prominence in the text It is hoped that such readily acknowledged bias will be treated kindly since it represents a deviation from the commonly accepted but equally overweighed viewpoint favoring surgical therapy

In the third and last section of the volume are presented those anatomic physiologic and pharmacologic facts which pertain to and help explain the pathologic alterations underlying peripheral vascular disorders The physiologic basis for the various clinical tests and therapeutic procedures is also included Knowledge of such material is essential for proper understanding of the subject matter and if a

ACKNOWLEDGMENTS

I am grateful to Doctors H B Shumacker Jr A G Prandoni and O Julian who permitted me to draw freely upon their collection of photographs of vascular abnormalities and to the members of the Vascular Center of the Mayo General Hospital Galesburg Illinois for their help in working up the clinical material upon which the present volume in part is based Acknowledgment is also made of the use of the following figures from the photographic files of the Veterans Administration Hospital Hines Illinois 6-9 11 2, -5 -7 -8 30 32 34 35 37 28 41 48 49 5- 55 59 60 and 6-68 Other figures were obtained from the Army Signal Corps Photographic Laboratory Mayo General Hospital Mr Donald Johnson and other members of the Department of Medical Illustration of the University of Illinois College of Medicine were of great help in the preparation of some of the plates I wish to express my appreciations to Doctors B M Kaplan C R Cummins E R Priest L Markin A A Zimmermann A A Billings R Baer and S Berger for their painstaking examination of the contents of this volume and their criticisms and suggestions My thanks are likewise due to Sandoz *Pharmaceuticals* through whose generosity the reproduction of the color photographs was made possible Acknowledgment is made to the J B Lippincott Company for permission to utilize material which originally appeared in an article in *General Practitioner* I am grateful to my wife Louise F Abramson for her devoted untiring and indispensable assistance in the technical preparation of the manuscript and to Mrs Henry B Perlman for her excellent editorial criticisms of the subject matter Finally I am indebted to Mr Paul B Hoeber for his patience and encouragement during the formative stages of this volume

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Chicago Illinois

PART ONE

DIFFERENTIAL DIAGNOSIS OF SYMPTOMS AND SIGNS

CHAPTER

I. DIFFERENTIAL DIAGNOSIS OF PAIN IN THE EXTREMITIES

The complaint which most frequently compels the patient to seek medical advice concerning his extremities is pain Since there are many conditions both vascular and nonvascular which may be responsible for this symptom only through careful questioning can the basis for the discomfort be ascertained It is necessary to elicit an exact description of the complaint with regard to location factors which initiate exaggerate minimize or eliminate it duration after the causative agent no longer operates and the effect of external temperature and humidity Another important consideration is the individual s tolerance to pain which can be a sessed by observing his reaction to some standard and only slightly painful procedure such as venipuncture Finally the role of functional overlay must also be evaluated

Pain in the extremities may result from a number of different states The first consists of changes in the tissues themselves such as inflammation swelling transient ischemia of muscle and destruction of pain sensitive structures Respon sible for such alterations are cellulitis and abscess formation occlusive arterial vascular disorders local arthritis frostbite trench foot and diseases causing severe venous impairment A second cause is involvement of sensory nerves either in their cou se through the limb or after they leave it to reach the spinal cord Examples of such a mechanism are the causalgic states cervical arthritis protruded intervertebral disks expanding neoplasms and the various neurovascular syn dromes due to pressure on the brachial plexus through movement of the shoulder girdle (Chap XX) Inflammation of peripheral nerves should also be mentioned as an etiologic factor Finally pain may be experienced in the limbs as a result of impulses initiated in visceral structures and referred to the periphery In this category belong the complaints in the upper limbs observed with angina pectoris myocardial infarction pericarditis and possibly the shoulder hand syndrome In the following section emphasis is placed on those symptoms which are primarily due to local arterial impairment Vascular disorders of venous origin which pro duce pain as well as nonvascular conditions having the same effect are also brought into the discussion for purposes of differential diagnosis

There are certain types of pain which follow a reduction in blood flow to an extremity These are intermittent claudication rest pain associated with chronic or acute anoxia and rest pain due to nutritional disturbances However with the

should be supported by other clear-cut findings of an occlusive arterial vascular disease before the complaint is attributed to reduced muscle circulation

The time of onset and the site of intermittent claudication will depend upon the relative degree of impairment of blood flow to the different muscle groups When the circulation to both lower extremities is not affected equally pain will first develop in the limb with the greater reduction Absence of symptoms in an extremity does not necessarily indicate that its muscle circulation is normal particularly if the patient stops walking with the first appearance of pain in one limb Under such circumstances an impaired blood flow in the other extremity will not become apparent through the production of symptoms since the limited load placed on its local circulatory mechanisms is not sufficient to overtax their functional capacity In some instances pain will be experienced in the two lower extremities almost simultaneously from which it can be inferred that the degree of impairment in both is approximately the same

Involvement of Upper Extremities In the upper extremities the incidence of occlusive arterial vascular disorders is much less common than in the lower extremities Furthermore in the course of daily activity few situations arise in which a great enough work load is placed on the muscles of the forearms or arms to bring out impairment of local muscle blood flow However in the case of the individual who is required to utilize the arms to any extent reduced circulation in these sites will result in typical intermittent claudication The type of symptom with its relationship to exercise and rest is similar in all regards to that described for the lower extremities

Summary Intermittent claudication is a pain which may be experienced in any group or groups of muscles in the extremities during a period of physical activity It disappears soon after the exercise is terminated and its severity and duration are directly related to the magnitude of the work load It indicates inability of the local vascular mechanisms in the muscles to satisfy the transient but marked increase in metabolic needs of these tissues during a period of exercise

Situations or Clinical Entities Causing Intermittent Claudication

Since intermittent claudication is always due to tissue anoxia it can be found in a variety of unrelated conditions nonvascular as well as vascular (Table 1)

Normal Vessel. Intermittent claudication may occur in extremities with no local structural changes in the blood vessels as a result of a number of different mechanisms First it may be experienced by a normal individual if the work load is so great that the resulting rise in metabolic needs of the exercising muscles cannot be adequately met even by maximally dilated and unimpaired vessels and a highly efficient cardiovascular system The difference between such a subject and a patient suffering from an occlusive arterial vascular disease is the degree of exercise which initiates the pain

Another factor which has been considered on [illegible]

[illegible] lists of references to be found at the end of each chapter

possible exception of intermittent claudication, rarely are the symptoms so typical and specific that a diagnosis of an occlusive arterial vascular disease can be made solely on such a basis It is well to remember that even intermittent claudication may be present in nonvascular conditions (p 5)

INTERMITTENT CLAUDICATION

Characteristics of Symptoms

Intermittent claudication is a symptom complex characterized by pain in a group or groups of exercising muscles in the extremities * It is described either as a sense of tiredness or fatigue, a dull ache, a sensation of tightness or compression a cramp or a sharp pain At times it may be experienced as a feeling of numbness referred to the digits Inasmuch as this complaint is one of the first to result from organic involvement of the peripheral arteries its early recognition is important It is of interest to note that intermittent claudication is comparable to angina pectoris at least as far as response to exercise is concerned If both conditions are present in the same patient, ability to exercise will be limited by either factor depending upon which vascular bed has the greater impairment of circulation relative to tissue needs

Involvement of Lower Extremities Intermittent claudication in the lower extremities generally presents a typical clinical picture It is experienced after the patient has walked a certain distance at a specific speed and is never present while he is sitting or lying down Neither does it exist on standing except in the far advanced state In fact in almost all instances relief occurs when the patient stops the exercise and merely stands still However, shifting the weight of the body to the uninvolved limb or sitting down produces a more rapid cessation of the pain In any event, the symptoms are generally gone within 2 to 5 minutes after termination of physical effort provided the patient stopped walking soon after their appearance Prolongation of activity much beyond this point results in an increase in the recovery period However pain which lasts for hours afterward should make one dubious of the diagnosis of intermittent claudication Similarly cramps in the legs which are noted some time after effort as for example, when the patient is lying down are not due to vascular deficiency

Changing the load placed on the exercising muscles causes variations in the time of onset and degree of severity of intermittent claudication If a patient increases his pace climbs a hill or walks at a normal rate but carries a heavy package the functional capacity of the impaired circulation will be surpassed sooner and the pain will appear more quickly Conversely if the gait is slowed or if some of the load is taken off the involved extremity through the use of a cane the ground covered before symptoms appear will be increased

Intermittent claudication can appear in any of the muscle groups of the lower extremity It may first be noted in the small muscles of the foot and later in the calf which is the most frequent location Finally pain may be experienced in the thigh However the presence of such a symptom in this site alone is rare and

* For physiologic basis for the symptom see p 455 for the treatment see pp 143 and 194

Table 1 Differential Diagnosis of Conditions Producing Intermittent Claudication

Clinical entity	Abnormal signs in involved limbs	Abnormal findings elsewhere	Clinical history
Arterio sclerosis obliterans and throm boangiitis obliterans	Absent or reduced arterial pulsations & oscillo metric readings abnormal positional color changes reduced cutaneous temper ature Trophic changes may be present	Associated corona ry cerebral and renal involve ment most often observed in arteriosclerosis obliterans	
Postligation of main arterial channel	Absent or reduced arterial pulsations & oscillo metric readings abnormal positional color changes redured cutaneous temper ature Trophic changes may be present	None	History of injury to ves sels or of sur gical excision of A.V fistula or arterial aneurysm
Acquired arterio venous fistula	Reduced pulsations oscil lometric readings and lowered cutaneous temper ature distal to fistula continuous murmur with systolic accentuation and thrill over it Large venous channels proximal to it	Possible increase in heart size and at times signs of congestive heart failure	History of injury to main artery and associated vein
Postembolism or throm bosis of main arterial channel	Reduced pulsations oscillometric readings & lowered cutaneous temp signs of neuritic involvement foot drop stocking glove type of anesthesia or hypesthesia	Presence of auricu lar fibrillation myocardial infarc tion or dilated heart in case of embolism signs of arteriosclerosis elsewhere in case of thrombosis	Previous history of sudden onset of severe con- tinuous pain in involved ex tremity and later the appearance of intermittent claudication
Coarctation of aorta	Reduced or even absent pulsations and oscillometric readings in lower extremities	Notching of ribs cardiac murmurs hypertension upper extremities hypotension lower extremities large collateral vessels on chest back and abdomen	
Marked anemia	No signs of impaired local circulation	Signs of anemia – dilated heart murmurs even congestive heart failure	Laboratory confirmation of condition
Severe congestive heart failure	Some reduction in pulsa tions & oscillometric readings some cyanosis and coldness of digits	Typical findings of reduction in cardiac reserve	
Angiospastic disease	No signs of impairment of local circulation except during exercise when pulsations decrease or disappear in exercising limb	None	

a time when an increase is required and hence pain is produced In individuals with such a response, no signs of impairment in blood flow are noted at rest, in contrast with those suffering from an occlusive arterial vascular disorder However during exercise or shortly after its termination, reduced or absent pulsations and decreased oscillometric readings are generally found

There are several systemic conditions in which intermittent claudication may be present even though there are no local structural changes in the vessels For example, in a severe degree of anemia despite the fact that the arteries in the muscles can dilate normally in response to the stimulus of exercise, the number of circulating red blood cells is so small that the total quantity of oxygen reaching the exercising tissues per unit of time is inadequate for their metabolic needs Therefore pain is experienced[7] In congenital heart disease associated with unsaturation of the blood, the oxygen supply to the muscles may also be insufficient, thus producing a similar situation Patients with congestive heart failure complain of muscular tiredness after short bouts of exercise, probably as a result of a number of factors which contribute to tissue anoxia, such as, reduced cardiac output, local capillary changes, mechanical effect of edema, and perhaps altered tissue fluid content Finally, in coarctation of the aorta, intermittent claudication may be experienced in the lower extremities, most likely due to the circuitous pathway through collateral vessels that the blood must take before reaching the muscle arteries

Occlusive Arterial Vascular Disorders The most common cause for intermittent claudication is a chronic occlusive arterial vascular disorder such as thromboangiitis obliterans or arteriosclerosis obliterans Intermittent claudication may also be noted following ligation of a major artery because of extensive injury, or in the presence of an arteriovenous fistula if there is enough shunting of blood into venous channels to interfere with the local circulation of the muscles Excision of the fistula or of an arterial aneurysm may likewise initiate the complaint if the operation is performed before an adequate collateral circulation has had time to develop In all these conditions one finds the symptom of intermittent claudication associated with clear-cut signs of impaired local circulation such as reduced or imperceptible pulsations in the main vessels of the extremity, decreased or absent oscillometric readings at different levels on the limb and abnormal color changes with various positions of the extremity (Chaps II and III)

Situations with no Apparent Correlation Between Severity of Symptoms and Physical Findings In some patients the complaint of intermittent claudication is not supported by obvious signs of an impaired arterial circulation Besides the conditions already discussed, several other possibilities must be considered under such circumstances First, it is conceivable that the occlusive process is limited to the arteries supplying the muscles involved with the result that normal or perhaps only somewhat reduced pulsations are present in the main arteries in the limb[1] Obstruction of the deep femoral artery, for example might cause intermittent claudication in the adductor region of the thigh without apparent alteration in pulsations or oscillometric readings in the leg and foot Another possible reason for the lack of objective findings is that an early stage of an occlusive arterial vascular disease exists, and consequently the changes in the large vessels are not

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factors. For example, marked shortening of the Achilles tendon can be readily identified, and if it exists, simple calf stretching exercises may be sufficient to relieve the symptom

Other changes that may be noted in the presence of *intermittent limping* are paralysis of one or more groups of muscles and neurologic signs indicating the existence of an extrapyramidal lesion With *hypertonicity of all the muscles*, a low serum calcium may be found and in such a situation proper therapy may cause complete *disappearance of the symptoms* Again it is necessary to emphasize the possibility of the coexistence of local arterial impairment and nonvascular conditions, *particularly in the elderly* patient Under such circumstances, if only the obvious condition is treated therapeutic failure will follow

Pressure on Main Nerve Trunks or Sensory Roots. Irritation of large nerve trunks innervating the tissues of the extremities may cause symptoms which mimic intermittent claudication especially if pain is exaggerated by movement of the trunk or limbs In the case of the lower extremity entities eliciting such a response are herniated lumbar disk, lumbosacral disease and sciatica Of diagnostic import is the fact that in these disorders the pain may become worse on change in posture as from the horizontal to the upright position, and not particularly on walking It is generally experienced in the buttock and radiates down the lower extremity along the course of the sciatic nerve Furthermore there may be signs of pressure and irritation of nervous elements, such as reduced vibratory sense perception and decreased sensation to cotton wool and pin prick in the toes, absent or diminished Achilles tendon reflexes, signs of spasm of the muscles of the back, tilting of the pelvis and a positive Lasegue's sign.* On the other hand there are no findings to suggest impairment of arterial circulation Therefore no difficulty should be encountered differentiating the pain associated with these entities from *intermittent claudication limited to the muscles of the thigh*

In the upper extremity pain from irritation of peripheral nerve trunks is pri*marily due to one of the disorders resulting from movement of the shoulder girdle* Among these are the cervical rib and scalenus anticus syndrome, the hyperabduction syndrome and the *costoclavicular syndrome In each instance symptoms are* produced when the brachial plexus and the subclavian artery are compressed by the assumption of the critical position for the specific entity, *while exercise of the* limb does not necessarily have any effect This is in contrast with intermittent claudication The existence of complaints and findings *suggestive of irritation of* peripheral nerves helps further in differentiating this group of conditions from occlusive arterial vascular disorders of the upper extremity *The pulse at the wrist* is generally normal except when the precipitating position causes it to become imperceptible as a result of temporary obliteration of the subclavian artery

Arthritic Changes The pain associated with arthritic changes is articular or periarticular in location It may be experienced at rest or may *follow immediately* after motion of the joint is initiated If present in the small joints of the fingers it may produce numbness and tingling The x ray is of use *in the differential diag*

* The test is performed as follows With the patient lying supine the leg is extended at the knee and the thigh is flexed at the hip A positive response is the elicitation of pain along the distribution of the sciatic nerve

nosis since it may show bony changes characteristic of the various types of arthritis Signs of vasospasm such as coldness cyanosis and hyperhidrosis may be present in certain cases of rheumatoid arthritis but these can be readily distinguished from the findings of obliterative vascular disease through use of various tests advocated for this purpo e (Chaps II and III) The observation that in arthritic conditions all the main peripheral arteries are intact and demonstrate normal pulsations and confirmation of this by oscillometry are of great help in the differential diagnosis

Avitaminosis Severe vitamin B_1 deficiency may be associated with symptoms in the extremities which resemble intermittent claudication At first the ability to walk short distances is unimpaired but when more prolonged exercise is attempted weakness may become apparent Not infrequently a history will be elicited that [illegible]

REST PAIN

Aside from intermittent claudication arterial impairment may be associated with several types of rest pain in the extremity In one the causative agent is a slowly progressing state of anoxia the symptoms in great part being related to the production of an ischemic neuritis The latter change is commonly found in patients suffering from arteriosclerosis obliterans and less often from thromboangiitis obliterans Another kind of rest pain follows acute anoxia of tissues resulting from sudden occlusion of a main artery to a limb by a thrombus or an embolus (p 149) Finally the appearance of trophic changes is invariably associated with pain locally In the presence of the above symptoms invariably there are clear-cut findings of a severe degree of arterial impairment in the involved limb

Rest pain in vascular disorders may be dependent upon other factors besides arterial insufficiency on an organic basis For example in the initial stage of trench foot immersion foot and posttraumatic vasomotor disorders the patient may complain of a severe degree of burning and excessive warmth because of reactive hyperemia The same type of response is experienced by the [illegible] at times, edema

REST PAIN IN THE ABSENCE OF NUTRITIONAL DISTURBANCES*

Ischemic Neuritis

Complaints due to ischemic neuritis are generally present at night while the patient is in bed and rarely during the day The explanation for this type of response is not clear although it may be related to the fact that at night the lack of

* See Table 2 p 16

factors For example, marked shortening of the Achilles tendon can be readily identified, and if it exists simple calf stretching exercises may be sufficient to relieve the symptom

Other changes that may be noted in the presence of intermittent limping are paralysis of one or more groups of muscles and neurologic signs indicating the existence of an extrapyramidal lesion With hypertonicity of all the muscles, a low serum calcium may be found and in such a situation proper therapy may cause complete disappearance of the symptoms Again it is necessary to emphasize the possibility of the coexistence of local arterial impairment and nonvascular conditions, particularly in the elderly patient Under such circumstances, if only the obvious condition is treated therapeutic failure will follow

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the muscles of the calf develops At the same time no signs of impairment of arterial circulation in the limb are observed

Since diabetes mellitus appears to be related to the early onset of generalized arteriosclerosis not infrequently peripheral neuritis resulting from this condition will exist in conjunction with arteriosclerosis obliterans Under such circumstances

may also produce pain at rest Among these are myositis fibrositis, and cellulitis Of interest is the adductor longus syndrome in which there is spasm and tenderness of the abductor longus muscle resulting in pain in the groin[8] The syndrome may follow pathologic changes in the myofascial tissue or be initiated reflexly from a distant lesion such as carcinoma of the lumbar spine or osteoarthritis of the hip In polycythemia, pain in the limbs may be very troublesome and severe It may take the form of numbness and tingling in the fingers and less often in the toes The symptoms have been attributed to local pressure on the bone from swollen hyperplastic bone marrow[3]

Little difficulty should be encountered in differentiating the symptoms produced by any of the above conditions from those due to arterial insufficiency However, it is well to remember that

... x-ray study and blood chemistry

... partial destruction ... limb will frequently ... very severe rest pain An example of local involvement is causalgia or the causalgia like states A neuroma formed at the site of traumatic section of a peripheral nerve may elicit a similar clinical picture as will certain occupations in which continuous pressure is applied in the vicinity of a sensory nerve Among possible etiologic factors producing pressure on nerve trunks in their course proximal to the extremity are arthritis of the spine, bursitis, neurofibromatosis neoplasms within the spinal canal, and herniated nucleus pulposus Abnormal sensations in the extremities may also follow a cerebrovascular accident involving the thalamus (thalamic hyperpathia)

Another state in which symptoms result from pressure on peripheral nerves is relaxation of the shoulder girdle muscles during sleep (brachialgia statica paresthetica[4] acroparesthesia) Because of compression of the brachial plexus by a normal first rib rest pain paresthesia and anesthesia are experienced in the upper extremity The syndrome is entirely sensory in its symptomatology (For further discussion see p 348)

Night Cramps A ...
muscle of the calf ...
During the attack ... the patient ... considerable pain which is relieved by massage of the

other stimuli permits the patient to become more acutely aware of the difficulties in his limbs Still, this fails to explain why he may be aroused from his sleep by the severe pain Another possibility is that while in bed there is a normal drop in blood pressure, which, in the case of the patient with occlusive arterial vascular disease, produces even further reduction in blood flow through partially occluded vessels Consequently, the peripheral nerves, already in a chronic state of anoxia, become more irritated, with resultant initiation or aggravation of neuritic symptoms

Complaints associated with ischemic neuritis possess certain characteristics typical of stimulation of nervous elements They are described as either a severe lancinating sensation which travels down the extremity, or as paresthesia formication burning prickling tingling or sense of numbness or coldness in the digits The symptoms may be sufficiently severe to interfere with sleep, causing the patient to suffer from lack of proper rest He soon learns however, that he will experience relief if he allows his feet to dangle over the edge of the bed or if he arises and walks around the room Attempting to sleep in a reclining chair may become a practical solution to the problem of obtaining enough rest, at least until swelling of the involved foot makes its appearance Besides definite signs of arterial impairment the patient suffering from ischemic neuritis may demonstrate some findings suggesting involvement of the peripheral nerves (For further discussion see *Abnormal Neurologic Signs*, Chap VI)

Symptoms Simulating Ischemic Neuritis

Peripheral Neuritis The pain of peripheral neuritis, due to diabetes mellitus or other causes is somewhat similar to that experienced by the patient with arteriosclerosis obliterans who is suffering from ischemic neuritis However it is generally much more marked and may involve all four limbs instead of the lower extremities alone as occurs in arteriosclerosis obliterans Complaints usually consist of a sense of heaviness paresthesias numbness or burning in the digits or the rest of the hand and foot, and lancinating pains Some patients compare their symptoms to the ones that would be experienced on walking on wood blocks or barefooted on pebblestones The individual with a severe degree of peripheral neuritis may not be capable of performing such acts as driving a car because of his inability to apply proper pressure to the pedals The symptoms are present continuously during the day as well as at night This is in contrast to the ischemic neuritis of arteriosclerosis obliterans in which pain is experienced primarily at night Furthermore uncomplicated peripheral neuritis is not associated with intermittent claudication

In this condition definite neurologic abnormalities are generally present Calf muscle tenderness and hyperesthesia of the leg ankle, and plantar surface of the foot are usually the earliest findings Loss of vibration sense perception in the toes may also be noted As the condition progresses Achilles tendon reflexes and later, patellar reflexes are lost In the far advanced case position sense in the toes becomes impaired sensory and motor changes are more apparent and atrophy of

Rest Pain of Nutritional Disturbances

Characteristics of Complaints

An ulcer or gangrene due to an impaired arterial blood supply invariably produces pain in the invol[illegible]
tinuous, although at ti[illegible]

walking due to stretchi[illegible]
ated from intermittent claudication in which pain is present only with physical effort Furthermore in the latter condition the complaint is localized to exercising muscles and not to regions demonstrating trophic changes

In the preulcerative or pregangrenous stage some difficulty may be encountered in making the proper diagnosis At times there may be few localizing findings except the pain referred to a portion of the extremity Usually, however the site of involvement manifests definite skin color changes, such as irreversible cyanosis or a reduced cutaneous temperature as compared with the surrounding skin After obvious ulceration or gangrene has occurred there can be little doubt as to the cause of the pain In either stage confirmatory evidence of the presence of a markedly impaired cutaneous blood flow is readily obtained by physical examination

Symptoms Simulating Pain of Ulcers of Arterial Origin

Ulcers of Venous Origin The pain associated with ulcers of the legs due to venous stasis is generally much less intense than that observed with the nutritional disturbances resulting from impaired arterial circulation It is described as a burning throbbing or aching sensation which *in most instances is not* severe enough to interfere with sleep Occasionally the pain may be quite disabling assuming the characteristic of a causalgia like symptom probably because of local irritation of the sensory component of the neighboring peripheral nerve by the inflammatory process In the majority of cases the symptom is *reduced* by bed rest with elevation of the limb to facilitate venous drainage while with dependency it is accentuated By contrast in the case of an ulcer of arterial origin raising the extremity may increase the severity of the *pain since this* position produces further decrease in arterial inflow and hence greater anoxia of the local nervous elements Another factor which influences the complaints resulting from a venous ulcer is the amount of infection that is present in the lesion and surrounding tissues Once this has been controlled the pain becomes less *marked* The presence of signs of impaired venous circulation such as pitting edema brown pigmentation varicosities and dilated veins and the absence of findings of a reduced arterial circulation are of importance in differentiating the pain associated with the ulcer of venous origin from that due to other cause

spastic muscles or by jumping out of bed and walking around the room The symptom generally lasts from several to twenty minutes or longer and may recur either many times in a single night or as infrequently as once a month

Night cramps exist in a number of unrelated conditions, as well as being experienced by otherwise normal individuals They may be part of the clinical picture of an occlusive arterial vascular disease, or more often, of venous stasis, as occurs in the postphlebitic syndrome or in varicosities The frequency of attacks appears to be directly related to the extent of physical activity indulged in on the preceding day Aside from vascular disorders, night cramps may also be initiated by hyperphosphatemia as in pregnancy, by hypocalcemia and by hypochloremia produced in the cardiac patient on a rigidly restricted salt intake who is receiving intensive diuretic therapy Individuals who have lost a considerable amount of fluids and salt, as by vomiting, severe diarrhea, or from profuse sweating are likewise prone to experience them Night cramps may be present in hypertensive patients

The mechanism which precipitates the attack in the leg is evidently the involuntary stretching of the Achilles tendon during sleep A similar type of reaction is responsible for cramping in the toes The underlying basis for the response is not clear, but it may be related to an increase in irritability of the neuromuscular junction, due either to an accumulation of metabolites or to a local alteration in metabolism (For treatment, see *Night Cramps* Chap XVI)

The significance of night cramps depends upon the other findings, this complaint alone having no clinical import If there is definite evidence of venous involvement, such as a history of deep thrombophlebitis the existence of edema varicosities, and pigmentation, then the symptoms must be attributed or related to venous stasis If there are clear-cut findings of impairment of the arterial circulation it may be explained on this basis

Pain on a Functional Basis Rest pain in the extremities for which there is no apparent organic basis is a fairly common complaint which presents a perplexing problem in differential diagnosis In the upper extremity it may take the form of numbness and paresthesias of the fingers which are experienced under various circumstances (restless hands hands going to sleep) In some instances the difficulties exist at night being severe enough to awaken the patient, while in *others they are experienced in the course of daily activity* Such *complaints* are rather common occurrences in young women and in many instances, despite a careful examination no signs of vascular neurologic or orthopedic dysfunction can be uncovered In the lower extremities the condition may take the form of nocturnal jerking (jitter legs) or an inability to find a comfortable position for the limbs in bed (restless legs) The symptoms may interfere with the patient s rest and are very difficult to control [7] There is little question that nervous fatigue and emotional tension can be wholly responsible for them Nevertheless such a functional basis should be entertained only after all possible organic causes have been eliminated in the differential diagnosis

Table 2 (continued)

Clinical entities in which symptom is found	Etiologic factor or pathogenesis	Conditions under which symptom is experienced	Effect of other conditions	Description of pain	Location	Signs of arterial or venous impairment	Neurologic findings
Psychoneuroses normal individuals	Maintenance of limb in one position for prolonged period of time	Lying down or sitting in case of hands holding an object for any period of time	Activity relieves symptoms	Uncomfortable sensation difficult to describe numbness paresthesia (restless hands and feet)	Digits and hand forearm foot and leg	None	None
Causalgic states neuroma occupational pressure on nerves	Injury of or pressure on peripheral nerves in limb	Rest	Slightest activity markedly exaggerates pain	Severe excruciating lancinating burning pain	Hand or foot	Signs of increased sympathetic tonus	Signs of partial destruction peripheral nerves
Posttraumatic vasomotor disorders	Injury of other tissues in limb	Rest	Activity exaggerates pain	Severe continuous	In hand or foot	Signs of increased sympathetic tonus	None
Rheumatoid arthritis osteoarthritis acute rheumatic fever	Local changes in joints	Movement of involved joint also present at rest	Rest relieves pain to some extent	Dull or sharp	In vicinity of involved joint or joints	Signs of increased sympathetic tonus in some instances	None
Glomus tumor	Dilated vascular channels with pressure on nerves in vicinity	Local heat trauma cold dependency	Elevation or normal environmental temp relieves pain	Excruciating burning	Around nailbed of digits	None	None

Table 2 Differential Diagnosis of Pain in the Extremities

Clinical entities in which symptom is found[a]	*Etiologic factor or pathogenesis*	*Conditions under which symptom is experienced*	*Effect of other conditions*	*Description of pain*	*Location*	*Signs of arterial or venous impairment*	*Neurologic findings*
			I LOCATION IN BOTH UPPER AND LOWER EXTREMITIES				
A o & t a o a v fistula postligation or occlusion of main arteries coarctation of aorta marked anemia	Transient muscle ischemia	Exercise of muscles	Standing sitting & lying down relieve symptom	Fatigue ache cramp sense of numbness in digits (intermittent claudication)	Muscles of upper and lower extremities	Arterial involvement invariably present in occlusive arterial vascular diseases but not in other entities	Minor ones may be present
T a.o a o Raynaud s disease postarterial embolism frostbite thrombosis associated with cervical rib or infectious diseases	Trophic changes of arterial origin (ulcer or gangrene)	Rest	Pain aggravated by moving involved portion	Sharp continuous or intermittent at times excruciating at other times mild	In vicinity of ulcer or gangrene	Arterial involvement severe either large or terminal vessels affected	Minor ones may be present
Sudden occlusion of main artery by embolism or throm bosis	Acute anoxia of tissues	Rest	Pain exaggerated by movement	Severe continuous excruciating numbness & paresthesia	Digits and foot or hand	Arterial involvement invariably present	Anesthesia hypesthesia in severe type foot & wrist drop
Polyneuritis toxic neuritis post-trench foot & frostbite	Peripheral neuritis	Rest	Little change with activity	Paresthesia numbness burning sense of swelling	Fingers and toes	None	Hypesthesia anesthesia loss of vibration sense perception may be present

[a] *T a o* - thromboangiitis obliterans *a o* - arteriosclerosis obliterans

Table 2 (continued)

Clinical entities in which symptom is found	*Etiologic factor or pathogenesis*	*Conditions under which symptom is experienced*	*Effect of other conditions*	*Description of pain*	*Location*	*Signs of arterial or venous impairment*	*Neurologic findings*
Superficial benign thrombophlebitis *superficial migratory thrombophlebitis*	Acute occlusion of superficial veins	Movement of involved part or pressure over it	Rest relieves pain	Moderate dull or sharp pain	Legs thighs forearms	Signs of superficial venous thrombosis	None
Axillary vein thrombosis thrombosis of popliteal or iliofemoral vein	Acute occlusion of main venous channels	Rest	Movement exaggerates symptom	Severe constant pain dull at times	Along course of vein	Swelling vasospasm distension of superficial veins	None
Herpes zoster neurofibroma, radiculitis fracture of vertebra Paget s disease displaced disk osteoarthritis	Pressure on *nerve root* at intervertebral foramen irritation of posterior *root* ganglion	Rest	Movement *may exaggerate* pain	Burning	Entire extremity	No gross changes other than vasospasm at times	Present in some instances
Erysipelas cellulitis associated with *dermatophytosis*	Acute cellulitis	Rest	Movement exaggerates pain	Intense pain	In site of lesion	*None*	None
			II LOCATION IN LOWER EXTREMITIES ONLY				
Shortening of Achilles *tendon & gas*trocnemius paralysis of a group of muscles tetany extrapyramidal tract involvement	Paralysis or shortening *of muscles* alterations in neuromuscular junctions	Exercise	Sitting or lying down relieves symptoms	Cramplike pain or sense of exhaustion	In calf	None	*Signs of extrapyramidal tract involvement may be present*

Table 2 (continued)

Clinical entities in which symptom is found	*Etiologic factor or pathogenesis*	*Conditions under which symptom is experienced*	*Effect of other conditions*	*Description of pain*	*Location*	*Signs of arterial or venous impairment*	*Neurologic findings*
Dermatomyositis nonspecific myositis myositis associated with systemic infections polyarteritis nodosa	Myositis	Movement of muscle group local pressure	Rest and heat relieve pain	Dull ache at times severe	In involved muscle group	No gross findings	None
Erythromelalgia early state of trench foot and frostbite	Exposure to heat	High environmental temperature or rise in body temperature	Dependency accentuates elevation & immersion in cold water relieve pain	Severe burning	Hands fingers feet toes	None	None
Normal individuals sequel deep thrombophlebitis a o and t a o calcium deficiency sudden loss of fluids and salt	Stretching of muscles of limb	Lying on bed or sitting	Standing walking or massage relieves pain	Severe cramplike pain generally while in bed (*night cramps*)	Generally in calves less *often in feet* hands thighs forearms	None except in case of occlusive arterial vascular disorders	None
A o t a o polyarteritis nodosa	Ischemic neuritis	Rest lying in bed	Dependency usually relieves pain occasionally it exaggerates it standing or walking relieves it	Paresthesia lancinating pain burning sensation sensation of extreme coldness	Toes fingers	Signs of arterial involvement in case of thromboangiitis and arteriosclerosis obliterans	Mild changes

Table 2 (continued)

Clinical entities in which symptom is found	Etiologic factor or pathogenesis	Conditions under which symptom s experience d	Effect of other conditions	Description of pain	Location	Signs of arterial or venous impairment	Neurologic findings
III LOCATION IN UPPER EXTREMITIES ONLY							
Cervical rib and scalenus anticus syndrome hyperab duction syndrome costoclavicular syndrome pressure of glands or tumors	Pressure on brachial plexus and subclavian artery and vein	Movement of arms and shoulders in differ ent posi- tions	Return to resting position relieves pain	Numbness paresthesia	Fingers hands forearms	Temporary oblit eration of pulse on assumption of responsible position at times permanent occlusion	Hyperesthesia anesthesia
Angina pectoris myocardial infarc tion shoulder hand syndrome?	Referred pain	Physical activity also at rest	Rest causes relief in case of angina	Numbness	Inner sur face of arm and forearm ulnar side of hand	None	None

Table 2 (continued)

Clinical entities in which symptom is found	*Etiologic factor or pathogenesis*	*Conditions under which symptom is experienced*	*Effect of other conditions*	*Description of pain*	*Location*	*Signs of arterial or venous impairment*	*Neurologic findings*
Sciatica lumbosacral disease	Pressure on nerve plexus or root	Change in position from lying down to standing	Activity doesn t particularly affect pain	Radiating pain	Along course of sciatic nerve	None	Absent Achilles tendon reflex & loss of sensation in toes may be noted
Pes planus metatarsalgia	Alterations in the dynamics of the foot	Standing	Walking may increase pain somewhat lying down or sitting relieves it	Dull	Foot	None	None
Varicosities postphlebitic syndrome	Trophic changes of venous origin (ulceration)	Rest	Activity exaggerates pain	Sharp pain or dull ache	Generally around med malleolus	Signs of venous stasis	None
Severe varicosities postphlebitic syndrome	Venous stasis	Standing dependency	Elevation relieves pain walking reduces it somewhat	Aching heaviness tiredness	Leg and foot	Signs of venous stasis	None

CHAPTER

II PROCEDURES FOR STUDY OF ARTERIAL CIRCULATION IN THE EXTREMITIES

I TESTS REFLECTING STATE OF CUTANEOUS ARTERIAL CIRCULATION

In most instances the presence of abnormalities affecting the arterial side of the vascular tree can be readily ascertained through the use of several clinical tests These have for their primary purpose (1) evaluation of the state of the cutaneous circulation (2) determination of the degree of involvement of the main arteries (3) study of the influence of vasospasm or (4) survey of the muscle circulation A detailed description of the procedures suitable for bedside or office use is presented below and in Chapters III and IV while those that require hospital facilities or special apparatus will be found in Chapter XXV (For the physiologic basis for the tests see Chap XXVIII)

It must be pointed out that utilizing one group of tests alone is inadequate and may be misleading For example measures which reflect the state of blood flow through the large arteries are of little or no help in determining the extent and efficiency of the collateral circulation As a result information so obtained might suggest a poorer prognosis than warranted Only by integration of all the information made available through use of the various clinical tests can one arrive at a comprehensive evaluation of the state of the arterial circulation The procedures are presented in this and in the subsequent two chapters in the order in which they should be carried out A summary of the tests for both arterial and venous circulation is given in Table 6 p 66

INSPECTION AND PALPATION

Nutritional Disturbances

Signs of Ulceration or Gangrene The first step in the study of the cutaneous circulation of an extremity is inspection of the skin to determine whether or not there are signs of trophic changes Healed depressed scars on the digits loss of

Table 3 Points of Interest in Peripheral Vascular History

Difficulty in walking or pain in upper extremities with exercise (intermittent claudication) as related to factors which *precipitate* exaggerate minimize or eliminate symptoms localization of complaints effect of medication

Rest pain in the extremities type

Frostbite trench foot or other injuries leading to cold sensitivity and hyperresponsiveness to low environmental temperature

Nutritional disturbances such as ulceration gangrene loss of subcutaneous tissue changes in consistency and texture of skin and subcutaneous tissue

Hair and nail growth alterations in degree of sweating and in skin temperature

Involvement of the venous circulation such as varicosities superficial or deep thrombophlebitis pulmonary embolism or venous stasis (pigmentation stasis dermatitis swelling stasis ulcer night cramps)

Infections in the extremities such as cellulitis lymphangitis and lymphadenitis repeated attacks of dermatophytosis

Nonvascular systemic disorders associated with manifestations in the extremities such as diabetes mellitus hypertension sickle cell anemia

Nonvascular local disorders associated with abnormalities in the extremities such as orthopedic neurologic or dermatologic conditions

Occupations which might produce vascular changes in the extremities such as use of pneumatic hammer those associated with possible injury of limbs

Habits such as tobacco smoking chronic alcoholism

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pression of coldness of the extremities Besides studying the hands and feet it is also necessary to palpate the proximal portions of the limbs

Alterations in Sweating

Hyperhidrosis The presence of excessive sweating is determined both by inspection and palpation The sweat glands are innervated by sympathetic fibers and hence hyperhidrosis in the absence of a warm environment or the need for heat dissipation generally indicates increased sympathetic activity Such a view is supported by an associated finding of vasospasm as characterized by coldness of the skin cyanosis and a subjective sensation of coldness However, the combination of hyperhidrosis and excessive vasomotor tonus may likewise be present in conjunction with an occlusive arterial disease such as thromboangiitis obliterans

There are also a number of physiologic and nonvascular states in which hyperhidrosis exists This response is elicited in normal people on exposure of the body to heat and a high humidity and after severe exercise It is a frequent concomitant of fevers due to tuberculosis pneumonia and septicemia An individual affected by anxiety fear or joy may demonstrate excessive perspiration while a similar but exaggerated type of reaction is noted in the patient suffering from an anxiety state or neurocirculatory asthenia Finally certain types of hyperhidrosis are congenital or familial

Anhidrosis Lack of sweating may be caused by a number of different mechanisms It can result from local involvement of the sweat glands as in atrophy of the skin or follow elimination of the control of the sympathetic nervous system through sympathectomy or complete destruction of a peripheral nerve * If a reduced blood supply exists on the basis of structural changes in the vessel wall the sweat glands will be affected by the state of anoxia and a decrease in the production of sweat will result Therefore in contrast with the cold wet extremity indicating vaso pasm the cold dry limb may be linked with a diminished peripheral circulation due to an occlusive arterial vascular disease Frequently with an increase in local circulation sweating will reappear

State of the Nails

Changes Produced by Vascular Disorders The condition and rate of growth of the fingernails and toenails may also give pertinent information regarding the state of cutaneous blood flow It has been shown that these structures undergo changes when the local circulation is impaired either as a result of permanent organic alterations in the vessels or of vasospasm [1] In occlusive arterial vascular disorders the history can generally be elicited that the nails do not need to be trimmed for months at a time because of their slow growth Deformity brittleness and pigmentation of these structures may be noted The nail may also increase in thickness and show parallel ridging (Fig 1A B) Improvement in peripheral circulation may be reflected in the disappearance of such abnormalities In vasospastic

* Irritation of somatic nerve fibers by external pressure or through trauma causing only partial loss of function may produce excessive sweating as a result of stimulation of the sympathetic components

portions of digits, or large healed ulcers on the leg and elsewhere covered by a thin parchment like skin should make one suspect a definite impairment of cutaneous blood flow The existence of superficial patches of ulceration or gan grene, or of more extensive involvement, makes this a very good possibility In this regard, it is important to examine carefully the skin between the toes, as well as the rest of the limb However before concluding that the nutritional disturbances are due to an impaired arterial cutaneous circulation, it is necessary to rule out such etiologic factors as venous or lymph stasis, trauma or burns in a limb with a normal blood flow, and various types of systemic conditions associated with the production of ulcers and gangrene in the extremities (For the differential diagnosis of clinical entities producing trophic changes, see Chap VII, especially Tables 10 and 11)

Alterations in State of Skin and Subcutaneous Tissue Of lesser, but still con siderable, significance in the determination of the state of the cutaneous circula tion are the texture and consistency of the skin and subcutaneous tissue In general, firmness and good elasticity of these structures suggest adequate nutrition while large areas of softness or flabbiness may imply an impaired blood supply Other unfavorable findings are thickening of the tips of the digits and piling up of scaly material at the junction of the nail plate and the fleshy portion of the finger or toe The absence of wrinkling of the skin over the joints of the fingers may be due to abnormal attachment of this structure to the subcutaneous tissue as in scleroderma

Alterations in Skin Temperature

Precautions in Obtaining Data Palpation of the extremity in order to deter mine skin temperature may give definite information concerning changes in cutaneous circulation * In evaluating the alterations it is necessary to consider the period elapsing between the time the patient came in from outdoors and the study of the limb Obviously, during the winter months even the normal extremity will remain cold for an interval after the patient has entered the office Hence one can not draw any definite conclusions from such a finding unless the low skin temperature remains for some time after exposure to a warm environment Per sistently cold feet in the summer may indicate the existence of either some degree of vasospasm an occlusive arterial vascular disorder or both The fact that the warming effect of wearing shoes and socks may make less prominent a difference in skin temperature between the two feet or among the toes on the same limb is another reason for waiting at least a half hour after the vascular examination is begun before attempting to obtain such information This is generally sufficient time for equilibrium with the room temperature to occur

Technic Gross determination of skin temperature is best performed using the dorsum of the examining hand or the ventral surface of the fingers It is important to compare corresponding sites since a difference in cutaneous temperature of identical areas on the two limbs has much more significance than the general im

* For the physiologic basis see *Alterations in Skin Temperature* Chap XXVIII

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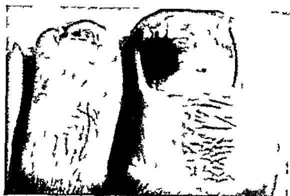
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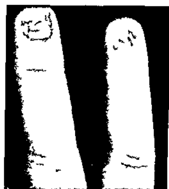
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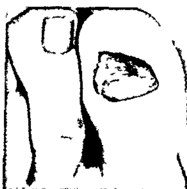












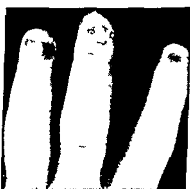


FIG 1 Nail changes in vascular and nonvascular disorders A Thromboangiitis *obliterans* B Arteriosclerosis *obliterans* C Raynaud's disease *showing pterygium* D Post trench foot syndrome showing pterygium E and F Onychomycosis G Psoriatic arthritis (A B C and D reproduced through the courtesy of E A Edwards Nail changes in functional and organic arterial disease *New England J Med* 239 362 1948)

conditions such as Raynaud's disease and posttrench foot syndrome the most frequent change is a thinning of the proximal nail fold with a gradual merging into the cuticle The latter structure is greatly widened joining almost imperceptibly with the nail to produce a lesion which has been termed pterygium (Fig 1C D)[2]

Spontaneous loss of nails may be due to undermining by local infection At times it may occur with no apparent basis as in severe Raynaud's disease The nails should always be scrutinized carefully for signs of subungual inflammation and tested for firmness of attachment to their bed

Changes Produced by Nonvascular Disorders The possibility that alterations in the structure of the nails might be due to nonvascular conditions must always be considered before implicating the peripheral circulation A common offender is a fungus infection (onychomycosis) Characteristically in this state the nail may be painful loose and brittle with a piled up irregular appearance at the free edge (Fig 1E F) The process begins with scaling of the nail under the overhanging cuticle and in time the whole nail plate may become involved The nail may turn yellow or dark brown or small chalky white spots may appear In onychomycosis due to monilia the disease begins under the lateral nailfold and pus may be expressed from beneath this structure Frequently onychomycosis exists in the presence of an occlusive arterial vascular disorder and under these circumstances difficulty may be encountered in determining the role played by each

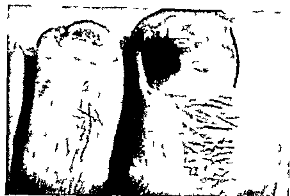
There are a number of other nonvascular diseases which cause changes in the nails Among these is hypoparathyroidism in which horizontal grooves and ridging commonly develop while the nails become white and crumbly and the nail plates separate Psoriatic arthritis is also associated with marked distortion of the nails (Fig 1G)

Growth of Hair

As in the case of the nails the growth of hair on the extremities is related to the state of nutrition of the tissues although in the presence of mild or moderate ischemia it may still be normal However in the limb with a markedly impaired circulation it may stop entirely Under these circumstances an improvement in blood flow may be followed by the appearance of new hair The presence of hair on involved toes may be of importance in determining whether such a procedure as amputation should be delayed in the hope that spontaneous healing of the nutritional disturbance might occur[2]

POSTURAL COLOR CHANGES

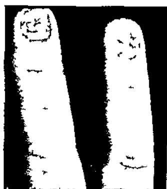
The second step in the determination of the state of the cutaneous circulation is the study of the change in skin color brought about by placing the extremity in various positions (Table 4) A very important prerequisite for this type of examination is the presence of a good light preferably from a natural source Artificial light will frequently distort the color changes (For the physiologic basis for normal and abnormal color changes see *Skin Color* Chap XXVIII)

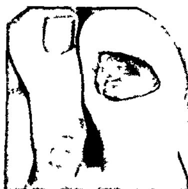












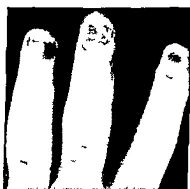


FIG 1 Nail changes in vascular and nonvascular disorders A Thromboangiitis obliterans B Arteriosclerosis obliterans C Raynaud's disease showing pterygium D Post trench foot syndrome showing pterygium E and F Onychomycosis G Psoriatic arthritis (A B C and D reproduced through the courtesy of E A Edwards Nail changes in functional and organic arterial disease *New England J Med* 239 362 1948)


A

B

C

D

E

F

G

H

I
J

Horizontal Position With the patient lying on the examining table and in a comfortable environmental temperature (around 23° C [74° F]) the digits of the normal hand or foot should demonstrate a slight flush Pallor, cyanosis (whether uniform or mottled) and rubor generally indicate the presence of some alteration of the local vascular system, especially when the response is limited to one limb or one or more digits (Fig 2A–E) It is necessary to note that skin color changes are significant in this regard only if one can eliminate such systemic conditions as congestive heart failure, the cyanotic type of congenital heart disease, a pneumonic process blood dyscrasias, carbon monoxide poisoning and shock

Elevated Position A convenient way to maintain the elevated position for the necessary period of observation is to have the patient clasp his hands behind his knees while the examiner lends aid by supporting the calves Care must be taken not to apply pressure in the vicinity of the popliteal artery Another means of taking the strain of this position off the debilitated patient is to have him rest his lower limbs on the back support of an armless chair which is placed inverted on the bed so as to form approximately a 45 angle with it

In the elevated position the extremities should remain pink to some degree Appearance of pallor in the distal portion of the limb is good evidence that a reduced arterial circulation exists If no change occurs in the case of the lower extremities it is necessary to have the patient dorsiflex his feet repeatedly, or in the case of the upper extremities, clench and open his fists, while the limbs are still held in the elevated position Then the feet or the hands are brought down to the level of the examiner s eyes and the ventral surfaces are observed and compared This added maneuver may bring out a pallor of the feet[4] (*positive plantar pallor test*) (Fig 2F) or of the hands which was not obvious as a result of elevation alone, such a response also indicates the existence of a reduced arterial circulation in at least the distal portion of the limb The dorsal aspects of the extremity are studied at the same time and corresponding digits compared for variations in intensity of the normal pinkness or of the abnormal pallor Through careful survey valuable information can be obtained regarding the existence of arterial impairment confined to a digit or a larger part of a limb

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FIG 2 Color changes in the limbs produced by various positions and procedures A Raynaud s disease showing digital pallor following exposure to cold B Uniform cyanosis of acrocyanosis affecting entire hand and adjoining portion of forearm C Vasospastic state showing cyanosis limited to portions of digits D Marked rubor of thromboangiitis obliterans E Mottling of livedo reticularis F Pallor of plantar surface of left foot following elevation of limb and repeated dorsiflexion at ankle (positive plantar pallor test) in a patient with arteriosclerosis obliterans Right foot of another patient *with a normal circulation* G *Delay in return of color in right foot in dependency* after elevation to drain out blood Normal response noted in left foot Veins on dorsum of left foot collapsed those on the right normally distended Abnormal responses in left foot due to thromboangiitis obliterans H Cyanotic rubor noted in foot remaining in dependency for a time change is characteristic of occlusive arterial vascular disorders although also present in vasospastic states I *Reactive hyperemia test* Normal response in right foot marked delay in return of color in left foot J Histamine *wheal test* Triple response noted central wheal surrounded by a zone of uniform redness with a periphery of mottled redness

One precaution must be borne in mind in the interpretation of the plantar pallor test the observer must wait several seconds following termination of the movements of the feet before examining them for color changes At times even in the normal individual the skin may look pale immediately after the exercise is stopped but then the pink color returns shortly In the patient with a reduced arterial circulation the pallor will persist or become more accentuated

Dependent Position If the extremity which has been elevated for some time is now placed in the dependent position the pink color will normally return in 10 seconds or less (*time of return of color in dependency*) In the patient with arterial impairment however there is a delay in its reappearance to as long as 45 to 60 seconds or more (Fig -G) the color being irregular and patchy rather than uniform In the presence of varicosities this test is of little value since skin color under these circumstances will return almost immediately after the feet are placed in dependency This is the result of retrograde flow of blood into the subpapillary venous plexuses from veins with incompetent valves As a result the presence of an impaired arterial circulation producing a slow return of color may be masked by the rapid filling of the cutaneous vessels from the venous side of the circulation

The changes in skin color when the extremity remains in dependency are also of value in determining the state of the cutaneous circulation In the presence of impaired local blood flow an intense cyanotic rubor may slowly develop in the foot (Fig -H) This is generally observed in the extremity which manifests a delay in return of color when first placed in dependency *The occurrence of a rapid cyanosis with the change to this position indicates that the tone of superficial vessels is low or absent and that immediate pooling of blood is taking place in them* Slowly forming mild cyanosis without rubor does not have much significance and it may even be a *normal response*

SUBPAPILLARY VENOUS PLEXUS FILLING TIME

A simple test to determine the state of tonus in the minute vessels of the skin consists of applying firm digital pressure to the skin for several seconds and then studying the color changes produced by sudden removal of the finger Normally the procedure causes pallor of the *skin* as a result of displacement of blood from the subpapillary venous plexus locally into the surrounding and deeper tissues followed by a return of normal color within a second or two

Delay in the return of color may be noted in the presence of a [illegible]
inflow due either [illegible]
Reduced or ab[illegible]
cause a slow re[illegible] more than 4 or 5 seconds when vasomotor tonus has been removed may indicate the presence of organic arterial disease or of paralysis of the subpapillary venous plexus The reappearance of the pink color may take the form of an irregular and slow filling of the pale area from the periphery inward

The above test not only gives considerable information regarding the turgor of the skin but it also helps differentiate between living and nonliving tissues Application of firm digital pressure to an apparently cyanotic area with no ap

In case of an arterial or arteriovenous aneurysm the onset of the flush is generally delayed and its intensity is less even in the presence of a fairly adequate collateral circulation Nevertheless if the changes are noted within 2–3 minutes after removal of the arterial occlusion pressure (but with digital obliteration of the involved artery still maintained), the possibility is good that trophic alterations will not occur distally following aneurysmectomy Delays beyond this point can be considered a warning that surgery should not be carried out until a more effective secondary blood flow develops

HISTAMINE WHEAL TEST

Technic The extremity is placed in the horizontal position and about 0 1 cc of a 1 1000 solution of histamine acid phosphate is injected intracutaneously or pricked into the skin with a hypodermic needle at 5 different levels the dorsum of the foot the leg just above the ankle the leg at the middle of the calf the leg below the knee and the thigh just above the knee* The sites are examined either visually or by palpation for the appearance of a wheal (Fig 2I) A delay in the production of this change beyond the normal time range of 3–5 *minutes* is interpreted as indicating definite impairment of circulation in the absence of wheal formation the blood supply can be considered to be precarious There are various gradations in the magnitude of the reaction and these can be tabulated as an absent faint fair or marked response *

Clinical Application The procedure is of value in occlusive arterial vascular disorders in following the rate of progression of the pathologic process Since it gives pertinent information regarding the existence of impending gangrene it may be helpful in preventing useless surgery At the same time it may contribute to the proper decision in respect to the level of amputation of an extremity

Precautions in Interpretation of Results It must be borne in mind that the histamine wheal test is only of value in the elucidation of the state of the cutaneous circulation A normal response does not rule out the possibility of severe occlusive disease of the arteries in the muscle the converse also being true In addition the procedure does not differentiate between a reduced cutaneous blood supply due to excessive vasospasm and that consequent to structural changes in the blood vessels Hence it is essential to repeat all tests giving a delayed wheal reaction after vasomotor tonus has been temporarily removed

SUMMARY

Considerable information regarding the state of the cutaneous circulation of the extremities can be obtained merely through inspecting and palpating the skin and subcutaneous tissues and by observing the skin color changes produced by placing the limb in different positions by applying [illegible]tal pressure to the skin and by [illegible]

c [illegible] of time For the performance

c [illegible]atus is required Although more

[illegible] also give pertinent information

* [illegible] physiologic basis see p 497

pearance of transient pallor indicates that an irreversible change has occurred and that the involved site will ultimately develop superficial or deep gangrene Evidently, the blueness of the skin under these circumstances is due to extravasation of blood into the tissue spaces as a result of a marked increase in capillary permeability The latter response is probably a reflection of the severe degree of local anoxia

REACTIVE HYPEREMIA TEST

Technic The reactive hyperemia test may be helpful in diagnosing an arterial vascular disease and is of special importance in the determination of the degree of adequacy of the collateral circulation in a limb with an arteriovenous or arterial aneurysm *

An ordinary blood pressure cuff with a somewhat longer cloth band is wrapped snugly around the thigh or the arm, and the limb is elevated for several minutes to facilitate drainage of blood out of the subpapillary venous plexus While in this position, the cuff is pumped to above the patient s systolic blood pressure (*arterial occlusion pressure*) the time is noted and the extremity is returned to the horizontal position After three minutes the pressure is suddenly released by disconnecting the mercury manometer from the system, and the color changes in the limb are studied [3]

When it is necessary to determine the state of the collateral circulation in the presence of an arterial or arteriovenous aneurysm, certain modifications are necessary First, with the cuff applied above the lesion the test as described is carried out to obtain a baseline Then it is repeated except that just before the arterial occlusion pressure is released the aneurysmal sac and the proximal portion of the artery from which it arises are obliterated by digital pressure The latter is maintained for about 3 minutes after the pressure to the limb has been removed, in order to observe the color changes that occur as a result of blood flowing solely through collateral vessels

Types of Responses to Temporary Anoxia In the normal extremity a bright red flush appears at the level just below the cuff almost immediately after removal of the arterial occlusion pressure, the change progressing rapidly and uniformly down the extremity until it envelops the digits in a matter of 10–15 seconds The flush remains for 10 40 seconds and then recedes in the same order that it advanced over the skin The entire color alteration should be completed within 2 minutes

In structural disease or marked vasospasm the flush is delayed in its appearance spreads slowly and is patchy It may take 2 or 3 minutes to reach and include the skin of all the digits (Fig 21) some changing color later than others The flush may be cyanotic instead of red and may take much longer than normal to disappear A delayed onset of the flush with a diffuse development of the full color may mean almost complete occlusion of a large vessel in the presence of good collateral circulation

* The physiologic basis for this procedure is discussed in *Changes occurring after reversal of experimental anoxia* Chap XXVIII

of Color Changes in Extremities

Pallor		Characteristic of color change	Skin temp of distal portion of limb	Location of change	Signs of local impairment of arterial circulation
Effect of position on color change	*Responsible mechanism*				
Elevation accentuates dependency reduces color change	Decrease in cutaneous blood flow with emptying of subpapillary venous plexus	Constant change	Decreased	Digits and feet	Definite
Very little change	Marked decrease in cutaneous blood flow & emptying of subpapillary venous plexus	Constant change	Markedly decreased	Most marked in digits & distal part of limb	Definite
None	Spasm of digital artery preventing blood from flowing into digit	Intermittent in form of attacks	Decreased during stages of cyanosis & pallor increased during stage of rubor	Limited to digits	Reduced or absent arterial pulsations may be present in Raynaud s syndrome
		Uniform or mottled constant	Generally decreased	Hands & feet	Signs of vasospasm
		Constant only in dependency	Normal	Feet & toes of involved limb	None
		Present only during exposure to cold	Decreased	Digits & hands & feet	None
		Present only during exposure to heat or with raised body temp	Definitely increased	Hands & feet	None
		Present only during exposure to heat	Increased	Hands & feet	None

Table 4 Differential Diagnosis

Clinical entity	Cyanosis		Rubor	
	Effect of position on color change	Responsible mechanism	Effect of position on color change	Responsible mechanism
Chronic thrombo-angiitis obliterans & arterio-sclerosis obliterans	Dependency accentuates elevation reduces color change	Slowing of cutaneous blood flow	Dependency accentuates & elevation reduces color change	Possibly permanently open A V shunts
Embolism thrombosis or ligation of main artery	None	Marked slowing of blood flow or trapping of blood in subpapillary venous plexus		
Raynaud s disease or Raynaud s syndrome	None	Slowing of blood flow into digit possibly venous spasm	None	State of reactive hyperemia following period of tissue anoxia
Other conditions associated with vasospastic states[a]	Dependency accentuates color change	Slowing of peripheral blood flow due to spasm of vessels		
Venous stasis associated with varicosities	Present in dependency may be present in horizontal position also	Slowing of venous outflow venous stasis		
Exposure of normal limb to cold environment	Dependency accentuates color change	Slowing of peripheral blood flow increased tonus of vessels		
Erythromelalgia			Dependency accentuates & elevation decreases color change	Marked peripheral vasodilatation – arterioles capillaries
Exposure of normal limb to hot environment			No definite effect	Peripheral vasodilatation arterioles capillaries

(continued)

Pallor					
Effect of position on color change	*Responsible mechanism*	*Characteristic of color change*	*Skin temp of distal portion of limb*	*Location of change*	*Signs of local impairment of arterial circulation*
		Present constantly during period of inflammation	Increased in area of lesion	Around lesion	None
		Constant change	Decreased	In involved limb	Signs of vasospasm
		Uniform constant change	Normal	All limbs particularly distal portion	None
None	Reduction in number of RBC carrying oxygen	Uniform constant change	Normal	All limbs particularly in digits	None
None	Peripheral vasoconstriction decreased peripheral blood flow due to reduced cardiac output	Uniform constant change	Definitely decreased	All limbs	Marked reduction in peripheral pulses & vasospasm
		Uniform constant change	Normal or somewhat decreased	Hands and feet	Reduced arterial pulsations
		Uniform constant change	Increased due to fever	Distal portions particularly nail beds of all limbs	None

Table 4

Clinical entity	*Cyanosis*		*Rubor*	
	Effect of position on color change	*Responsible mechanism*	*Effect of position on color change*	*Responsible mechanism*
Local inflammation			Dependency may accentuate color change	Local vasodilatation of arterioles and capillaries
Rheumatoid arthritis & anterior poliomyelitis	Little effect	Reduced peripheral blood flow due to vasospasm		
Polycythemia	Little effect	Increase in number of circulating red blood cells poorly oxygenated		
Severe anemia				
Shock				
Congestive heart failure	Dependency accentuates color change	Slowing of peripheral blood flow		
Pneumonia	No effect	Greater quantity of reduced hemoglobin in arterial blood		

[a] Acrocyanosis livedo reticularis causalgia posttraumatic vasomotor disorders acute stage of deep thrombophlebitis and sequelae of this condition and acute and chronic stages of frostbite and trench foot

CHAPTER

III PROCEDURES FOR STUDY OF ARTERIAL CIRCULATION IN THE EXTREMITIES (*Continued*)

2. PROCEDURES FOR DETERMINING STATE OF MAIN ARTERIES

EXAMINATION OF PERIPHERAL PULSATIONS

One of the most important steps in a vascular examination is palpation of the main arteries in the extremities to determine their pulsations Every vessel that can be examined should be checked even though the changes appear to be limited to one limb

Before presenting the technic of study of the major vessels it is necessary to discuss the various states which are associated with alterations in the amplitude of peripheral pulsations (Table 5) Among these are systemic disorders affecting the heart and general circulation syndromes producing obstruction of the great vessels local abnormalities of nonvascular tissues and finally entities causing either structural or functional changes in the blood vessels themselves

Systemic Disorders Affecting Pulsations

Reduced Cardiac Output Of the various systemic disorders which [illegible] the [illegible]

[illegible] and in shock in all of which there may be a decrease or even absence of peripheral pulses In the presence of numerous premature contractions marked reductions in the amplitude of the pulse wave are frequently encountered In auricular fibrillation a slight degree of vasospasm superimposed upon the generally weak and variable pulsations may be sufficient to make them almost imperceptible particularly in the feet Such a possibility must always be kept in mind whenever the question of a sudden occlusion of a main artery by an embolus arise in individuals with this disorder

Alterations in Pulse Pressure Changes in pulse pressure will also affect the

concerning the cutaneous circulation, usually the initial routine vascular examination can be carried out without resorting to their use However, they are of value in determining the proper level for removal of a limb

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of the artery reducing its size A superimposed thrombus may then completely occlude the vessel Thromboangiitis obliterans likewise demonstrates such changes although the pathologic process is inflammatory rather than degenerative (For further discussion of these entities see Chap IX)

There are several other organic diseases which are associated with reduction or absence of peripheral pulses Among these is Monckeberg's sclerosis (p 138) in which there is a deposition of calcium in the media interfering with the normal distensibility and elasticity of the vessel and hence producing some damping effect on the pulse wave As a result the artery may be felt as a firm calcified cord Certain conditions which follow trauma to main vessels, such as an arteriovenous fistula ligation of a lacerated artery and thrombosis due to irritation of the intima generally also demonstrate a decrease in or loss of pulsations

Changes in Vasomotor Tonus Increased vasoconstrictor tone may damp pulsations in an artery by maintaining it in a greater than normal state of contraction It is possible for this response to be so marked that the vessel will go into a state of spasm with complete obliteration of the lumen Under these circumstances no pulsations will be felt

Inhibition of sympathetic control over peripheral arteries is followed by an increase in the amplitude of the pulsations due to passive dilatation of the vessels This type of response is noted transiently when there is need for heat dissipation as in the presence of fever or on exposure of the extremities to a high environmental temperature Bounding pulses are also seen in erythromelalgia in which there is an exaggerated response to a warm environment and in the early stage of trench foot frostbite and immersion foot as a result of reactive hyperemia Local inflammation is associated with a similar type of alteration Complete and relatively permanent removal of vasomotor influence through sympathectomy produces an increase in pulsations provided the vessels are capable of dilating

TECHNIC OF EXAMINATION OF PERIPHERAL PULSES

In the examination of the peripheral pulses it is necessary to compare the amplitude and force of the pulsations in one artery with those in the corresponding vessel on the opposite side The manner in which the data should be recorded depends upon individual preference The pulsations can be described as normal moderately or markedly reduced or absent or as ranging from 4+ to 0 with the former figure representing the maximal normal amplitude Only with experience can one determine what is a normal pulsation for any single artery (For anatomy of arterial tree in the extremities see Chap XXVI)

Precautions Taken in the Examination It is important that the observer is comfortable while examining for pulsations in the vessels Frequently the beginner in the field may be unsuccessful in palpating an artery merely because he assumes a position which places a strain on the muscles of his body with a resulting dulling of his perceptive senses A possibility which must also be kept in mind is that when firm pressure is utilized in feeling for the vessels the pulse in the finger of the examiner may be mistaken for the one in the artery of the patient This can be readily differentiated by having the observer count the beats aloud while another checks the rate against a different pulse in the subject preferably of

amplitude of the pulsations in the extremities These follow *alterations either* in the dynamics of the heart, in the peripheral resistance, or in both In such conditions as aortic stenosis constrictive pericarditis, pericardial effusion with tamponade and myocarditis, the pulse pressure is decreased and, as a result, the peripheral pulsations are weak On the other hand, in aortic insufficiency hyperthyroidism, severe anemia, and hypertension, the pulse pressure is increased and hence the peripheral pulses may be bounding and strong Such a response may also be noted in the normal individual undergoing physical exertion

Conditions Producing Obstruction of, or Pressure on Great Vessels

Involvement of the great vessels and their main branches will likewise result in changes in pulsations in the extremities For example, in coarctation of the aorta, the pulses in the femoral artery as well as those in the dorsalis pedis and posterior tibial arteries may be markedly diminished or even absent A similar situation exists in the case of thrombosis of the bifurcation of the aorta (*Leriche s syndrome* p 166) and in dissecting aneurysm of the abdominal and thoracic aorta Extrinsic pressure on the main vessels by tumors or other structures will produce the same type of change

It is apparent, therefore, that in the presence of any of the conditions in the above two categories all information obtained by palpation of the peripheral pulsations must be re-evaluated from the point of view of the amount of change contributed by distant influences If this is not done a distorted picture of the local circulation will be obtained

Extrinsic Factors Acting Locally

Besides the distant influences the pulsations in the peripheral arteries may also be affected by local changes in nonvascular tissues Among these are alterations in the thickness and consistency of the overlying skin and subcutaneous tissue, hypertrophy of the musculature covering the vessel and the presence of pitting and nonpitting edema In the case of pitting edema it may be necessary to apply firm digital pressure for a time over the site in which the artery is usually found before actually attempting to palpate it By this means the fluid covering the vessel is displaced and thus its pulsations may become apparent to the palpating fingers

Conditions Producing Local Changes in Vessels

If systemic effects and local abnormalities of nonvascular tissues can be ruled out, then variations in the amplitude of the arterial pulsations in the extremities must now be attributed to a change in the caliber of the arteries themselves This may take the form of either permanent structural alterations in the vessel wall or temporary vasospasm or vasodilatation, depending upon the type of modification of vasomotor control

Structural Alterations in Vessel Wall One of the most frequent causes of decreased or absent pulsations in the vessels of the lower extremities is arteriosclerosis obliterans In this disorder atheromatous plaques extend into the lumen

of the artery reducing its size A superimposed thrombus may then completely occlude the vessel Thromboangiitis obliterans likewise demonstrates such changes although the pathologic process is inflammatory rather than degenerative (For further discussion of these entities see Chap IX)

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while [illegible] e beats aloud
preferably of

Table 5 Conditions or States Affecting Amplitude of Peripheral Pulsations

Clinical entities or states in which change is present	*Underlying mechanism*	*Type of change*	*Other abnormalities in extremity*
Terminal stage of congestive heart failure paroxysmal tachycardia rapid auricular fibrillation numerous premature contractions shock	Reduced cardiac output	Reduction or absence of pulsations	Edema may be present in some instances vasospasm may be present
Aortic stenosis myocarditis	Decreased pulse pressure	Reduction in pulsations	None
Exercise hyperthyroidism hypertension aortic insufficiency marked anemia	Increased pulse pressure	Increase in pulsations	None
Coarctation of aorta Leriche s syndrome dissecting aneurysm of aorta cervical rib or scalenus anticus syndrome	Obstruction of or pressure on large ves sels proximal to limb	Reduction in pulsations	Other signs of impaired arterial circulation may or may not be present
Brawny induration pitting & nonpitting edema lipedema hypertrophy of muscles overlying vessels	Changes in nonvascular tissues of extremities	Reduction or absence of pulsations	Signs of venous stasis present in some instances
Thromboangiitis obliterans arteriosclerosis obliterans occlusion or ligation of main artery a v fistula	Structural changes in artery	Reduction or absence of pulsations	Other signs of impaired arterial circulation invariably present
After sudden occlusion of main vein during & after severe exercise in some individuals	Acute vasospasm	Reduction or absence of pulsations reappearance of normal pulsations after inhibition of vasomotor tonus or after rest	Other signs of impaired venous circulation in case of sudden occlusion of vein
Acrocyanosis, Raynaud s disease livedo reticularis posttraumatic vasomotor disorders posttrench foot syndrome arthritis poliomyelitis rheumatoid arthritis disuse atrophy	Chronic vasospasm	Pulsations may be reduced or normal	Other signs of vasospasm may be present
Erythromelalgia early stage of reactive hyperemia in frostbite trench foot & immersion foot exposure to a hot environment or a rise in body temperature inflammation postsympathectomy	Moderate to marked vasodilatation	Increased and bounding pulsations	Other signs of vasodilatation

the corresponding vessel on the opposite extremity Another precaution which should be taken is to vary the pressure depending upon the depth of the vessel below the skin In each instance too different degrees of pressure should be used successively for occasionally a weak pulsation may not be felt at all if the artery is palpated with force

Examination of Arteries in Upper Extremity In the upper extremity the *brachial artery* can be felt by encircling the arm in its lower third with the examining hand and pressing the tissues of the medial aspect of the limb against the bone as noted in Fig 3A Generally the pulsations can then be followed upward toward the axilla for some distance

The *radial artery* also presents no difficulty for the examiner when it is in its usual position on the anterior surface of the wrist medial to the styloid process of the radius However in an occlusive arterial vascular disease the distal portion of the artery may be completely obliterated while the segment above remains intact Therefore it is advisable to continue the examination proximally over the forearm when pulsations are not felt at the wrist

The *ulnar artery* can be felt at the same level at the wrist as the radial but on the opposite side It is generally situated more deeply and hence firm pressure is necessary to locate it At times however it may be as superficial as the radial It is palpated at the junction of the hand and the wrist as depicted in Fig 3B This vessel which lends itself to palpation almost as readily as the radial should be examined routinely

In certain instances the ulnar artery can be felt only with difficulty or not at all because of an aberrant location In all doubtful cases therefore the ulnar confirmatory test (*Allen's test*) is performed[1] The extremity is elevated to effect drainage of blood out of the small vessels of the skin and firm digital pressure is applied by the examiner to the radial artery at the wrist so as to obliterate it Then the subject opens and closes his fist a number of times with the arm in this position in order to facilitate further venous outflow With the compression still maintained the hand is brought down to the level of the heart and the fist is opened no attempt being made to extend the fingers fully The [illegible] The flush may cover the skin almost instantaneously or this may not occur for 20–40 seconds Both can be considered normal responses If however the palmar surface of the hand remains blanched as long as the pressure is maintained over the radial artery and if the color returns immediately on removal of the obstructing fingers this is good evidence that either the ulnar artery is obliterated by a disease process or some type of anatomic anomaly exists in the connection between this vessel and the volar arches [*] It is advisable to repeat the

[*] A similar procedure can be utilized to determine whether or not the radial artery is conducting blood when pulsations are not felt in the portion of this vessel at the wrist The steps are exactly the same except that the ulnar artery is digitally compressed instead of the radial The absence of flushing of the skin of the palm when the hand is placed at the level of the heart and pressure is maintained on the ulnar artery indicates that either the radial artery is occluded or the involvement is in the superficial or deep volar arch (For anatomy of these structures see *Arteries of the upper extremity* Chap XXVI)

test a number of times before deciding that the vessel is involved since on occasion, flushing may occur after two or three failures The explanation for this type of response is not clear

Examination of Arteries in Lower Extremity Examination of the arteries of the lower extremities, with the possible exception of the popliteal is accomplished without much difficulty The *femoral artery* can be readily felt in the groin below Poupart s ligament, as noted in Fig 3C Its pulsations are normally greater than those of any other vessel in either the upper or lower extremities

Palpation of the *popliteal artery* presents somewhat of a problem, since it is generally located quite deeply in the fatty tissues within the diamond of the

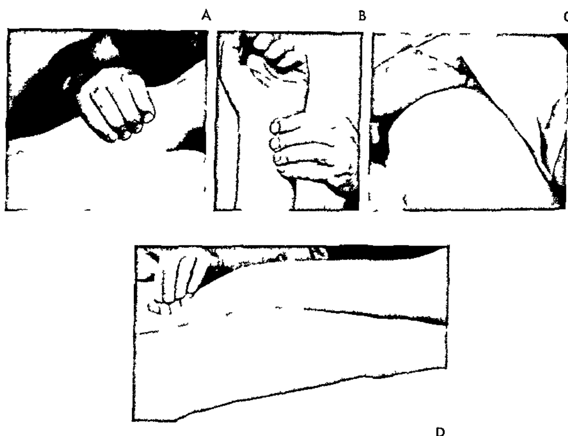


Fig 3 Appropriate positions for determining the state of pulsations in peripheral vessels A Brachial artery B Ulnar artery C Femoral artery D Popliteal artery

popliteal fossa Frequently the patient s inability to relax increases the difficulty A *satisfactory procedure for palpating for this vessel* is depicted in Figure 3D The patient lies prone and crosses the foot of the extremity being investigated over the back of the other limb thus relaxing the tissues traversing the popliteal space since the leg is now slightly flexed Deep pressure is required to feel the artery and this can be obtained by placing the fingers of the other hand over the examining fingers and pressing firmly In this manner the perceptive sense of the palpating digits is not dulled as would occur if these were performing the dual function of exerting force to compress the tissues and of seeking the vessel


E


F


G

Fig , (*Continued*) E Dorsalis pedis artery F Posterior tibial artery G Perforating branch of peroneal artery (From D I Abramson Practical procedures in bedside diagnosis of peripheral vascular disorders *General Practitioner* 6 546 1955)

Even with this procedure the pulsations of the popliteal artery can not be felt at times because of the deep location of the vessel Under these circumstances they may be detected by taking a blood pressure reading at the popliteal space using the auscultatory method with the sphygmomanometer cuff around the thigh in its lower position and the patient lying prone If sounds can be heard in the popliteal space as the pressure is lowered it can be assumed that the popliteal artery is present and patent

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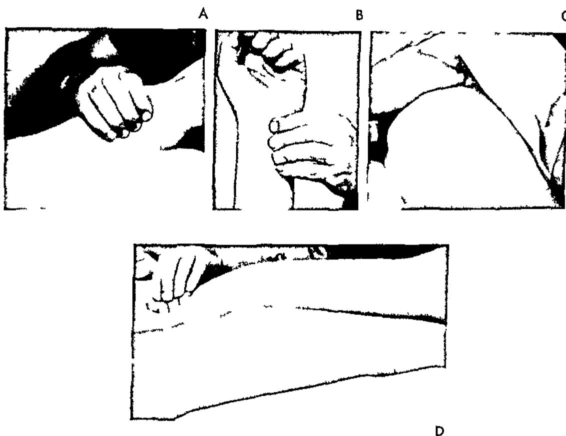


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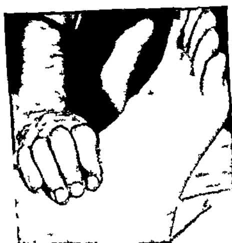
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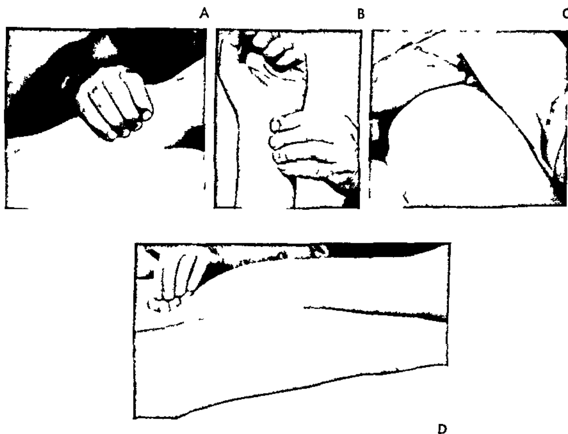


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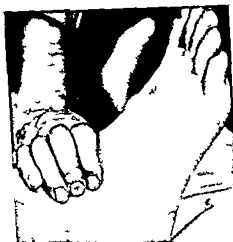


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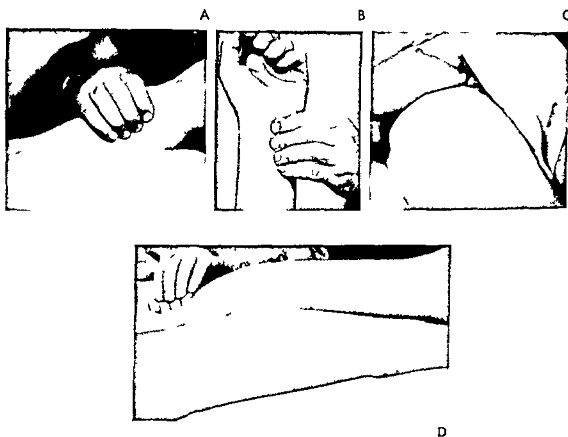


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Interpretation of Findings

Absence of pulsations in the main arteries of the extremities does not always have the same connotation For example inability to palpate the radial femoral or posterior tibial arteries generally indicates the existence of either an occlusive arterial vascular disease or marked vasospasm It is necessary to point out however that on occasion the posterior tibial artery may be impalpable behind a prominent medial malleolus often found in people with squat feet Similarly the popliteal artery may not be felt because of anatomic alterations in the popliteal fossa Obviously such a finding would have no significance in the presence of normal pulsations in the dorsalis pedis and posterior tibial arteries An occluded ulnar artery when definitely established by the ulnar confirmatory test is of diagnostic importance since it may be the first objective indication of thromboangiitis obliterans On the other hand the absence of one or both dorsalis pedis arteries has been reported as a normal variant in approximately 13 per cent of people[6] When it can not be felt it is advisable to palpate anteriorly over the ankle joint for the anterior tibial artery of which it is a continuation

OSCILLOMETRY

Considerable differences of opinion exist with regard to the value of oscillometry in peripheral vascular diseases Some workers believe that the test is of little use while others[3 5] consider it to be a very important part of a vascular examination On the basis of personal experience and observation it would appear that the latter opinion has much in its favor

TECHNIC

There are a number of satisfactory oscillometers available commercially (see Appendix) all of which will give reproducible results over the same site provided a routine method of application is utilized and similar basic conditions are maintained i e *constant* environmental temperature and emotional state of patient and equivalent periods of rest before readings are made It is advisable to have the patient lie on his back during the test and avoid manifesting any interest in the procedure In order to be able to compare findings obtained on a subject at different times it is necessary to use *the identical* apparatus since even those made by the same company may vary in their *sensitivity* Certainly comparison of data using instruments of different manufacture is of little value

Rationale fo Us The oscillometer consists of a modified pneumatic cuff connected to a sensitive aneroid which measures the pulsatile variations in size of limb with each cardiac systole These changes produce corresponding alterations in the air volume of the cuff which are transmitted to the aneroid where they cause an amplified swing of the attached needle The range of movement is noted on an arbitrary degree scale of the *instrument* Since the increase in volume of the limb is due to the fact that initially blood is entering the main arteries mo e rapidly than it can escape into the arteriolar bed the magnitude

vessel, although it is somewhat easier to palpate the right dorsalis pedis artery from the left side of the patient, using the right hand, as depicted in Fig 3E, and reversing the position and the hand in the case of the left dorsalis pedis artery The entire dorsal surface of the foot should be examined before deciding that the vessel is not present

The *posterior tibial artery* can be felt without much difficulty as it passes behind and beneath the medial malleolus In the case of the left foot, the examiner stands on the left side of the patient and cups the fingers of his right hand over the medial malleolus so that the finger tips slide off to enter the groove below as seen in Figure 3F In the case of the right foot, the opposite position and the left hand of the examiner are utilized Generally, rather firm pressure is necessary to feel the artery, the procedure being facilitated by simultaneously dorsiflexing the foot slightly with the other hand (Fig 3F), putting the vessel somewhat on stretch At times the posterior tibial artery can be seen pulsating below the medial malleolus This may be noted in patients in whom some peripheral arteriosclerosis is present, as well as in thin normal individuals

Variations in Technic to Bring Out Pulsations In cases in which the arteries in the feet are not palpable with the patient lying on his back it may be advisable to repeat the examination with him seated and the lower extremities in dependency and the observer sitting on a chair At times such a procedure will allow for the recognition of pulsations which could not be felt otherwise The explanation may be that in this position the hydrostatic effect of the column of blood now contributes enough to the reduced pulsations of the vessel to make them apparent to the palpating finger

On occasion, if the arteries are examined immediately following a period of exercise pulsations may be felt which were not obtainable during rest This is probably due to the fact that the increased cardiac output consequent to effort causes sufficient distension of a partially occluded vessel so that it becomes palpable However it must be borne in mind that in some individuals, spasm of normal vessels may occur with exercise and that under such circumstances, peripheral pulsations will now become less or even disappear rather than increase (p 5)

If signs of vasospasm are associated with absent pulsations it may be necessary to remove vasomotor control (by any one of the simple clinical means discussed in Chap IV) and re examine the pulses As has already been mentioned, hypertonus may affect large arteries to the point that the pulsations are practically imperceptible Temporary elimination of this factor will invariably cause them to return to a normal amplitude provided there is no other contributing state

Search for Aberrant Vessels In all instances, search should be made for the presence of anomalous arteries If there is difficulty in palpating the radial artery, examination should be directed to the dorsal surface of the base of the thumb for a vessel that may be taking over its function In the lower extremity, with obstruction of the popliteal artery the lateral or medial superior genicular arteries may become prominent in their course over the knee At times in the absence of the posterior tibial artery a large vessel may be present along the upper border of the lateral malleolus which is probably an enlarged perforating branch of the peroneal artery (Fig 3G)

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Insensitivity of Clinical Apparatus A limitation to oscillometry is the fact that the instruments available for clinical use are not sensitive enough to pick up oscillations in small collateral vessels in which the pressure is lower than in the main arteries of a limb Since in an occlusive arterial vascular disease, this secondary system frequently carries on the principal function of supplying the tissues with nutrition it is obvious that information derived from oscillometry alone would be of little value in determining the over all state of the local circulation Conversely, there could be structural impairment of the small arteries and arterioles distal to the main channels, leading to partial anoxia of the tissues, and still with no corresponding decrease in the oscillometric measurements of the limb Therefore, it can be stated that oscillometry is of little value in arriving at a *proper conclusion regarding prognosis*

VENOUS FILLING TIME

The rapidity with which the superficial veins of an extremity fill after having been collapsed gives pertinent information concerning the rate of arterial inflow into the limb The extremity is raised for several minutes, to drain the blood out of the surface vessels and then quickly lowered[4] The period required for the superficial veins on the dorsum of the hand or foot to become visible is recorded, a normal response occurring within 10 seconds after the limb is placed in dependency (venous filling time—Fig 2G p 28) * Delays beyond this time indicate some arterial impairment, although the test does not differentiate between a functional and an organic disorder unless it is repeated after vasomotor tonus has been removed (Chap IV) Furthermore if varicosities exist, in which case the superficial vessels fill immediately with blood coming from the deep venous system, or if the veins can not collapse when emptied of blood because of fibrous changes in their *wall* the results of the test are of no value and may in fact, lead to a false conclusion regarding the arterial circulation

SUMMARY

A study of the state of the pulsations in the peripheral arteries is of greatest importance in determining whether or not an occlusive arterial vascular disease exists This is accomplished first by palpation of the vessels and second by means of the oscillometer Such procedures as well as the test for determining venous filling time can be readily carried out at the bedside or in the office †

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* This interval generally parallels that necessary for the return of skin color after the limb is moved from the elevated to the dependent position (p -9)

† For the technic of and indications for arteriography and soft tissue x ray *see Chap XXV*

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CHAPTER

IV PROCEDURES FOR STUDY OF ARTERIAL CIRCULATION IN THE EXTREMITIES (*Continued*)

3 TESTS FOR REMOVAL OF VASOMOTOR TONUS AND FOR DETERMINATION OF STATE OF MUSCLE CIRCULATION

TESTS FOR REMOVAL OF VASOMOTOR TONUS

In the preceding two chapters, attention has been called to the fact that several of the tests described *do not distinguish between decreased circulation produced* by permanent structural changes in the wall of an artery and that which follows transient reduction in the size of the lumen as a result of excessive sympathetic tonus Since the latter state is much more amenable to treatment, it becomes of paramount importance to determine its role in the clinical picture For this purpose several procedures are available, each of which involves a study of the rise in cutaneous temperature of the extremities produced by temporary removal of sympathetic control It is postulated that such a change is a reflection of the increase in cutaneous blood flow that occurs when the vessels passively dilate the magnitude of the effect is related to the degree of vasomotor tonus present initially

Conditions and Apparatus Necessary for Proper Study of Cutaneous Temperature Changes

Temperature of Room Since dependable skin temperature readings are essential to the accuracy of the examination it is necessary to obtain these in a room in which all drafts are eliminated and the temperature is within physiologic limits i e between 20° and 25° C (68° and 77° F) There is no need for a constant temperature room at least during those seasons in which the outside temperature is equal to or less than the desired level * When it is higher then

* An effective means to reduce room temperature under such circumstances is to open a window sufficiently to allow an ordinary electric fan to be placed on the sill facing outward and then to block out the space on either side of the machine with cardboard The window is brought down from the top so as to leave a space above of a foot or so When the fan is turned on air currents are produced which result in cool air being brought in through the upper vent while warm air in the room is expelled through the fan blades

some type of simple portable cooling unit must be introduced to drop the temperature and reduce the humidity

Means of Recording Skin Temperature To determine the rise in skin temperature produced by removal of vasomotor tonus, a skin thermometer is necessary It may be argued that the purchase of such an apparatus is too expensive for the general practitioner or the internist who sees only an occasional vascular case Recently however a number of fairly inexpensive instruments have become available commercially which although not as accurate as the more elaborate ones used for research purposes, are adequate for clinical testing of vasomotor tonus (see Appendix)

In principle the apparatus consists of a sensitive galvanometer (millivoltmeter) on which are recorded the electrical currents generated when two sets of connected thermocouple junctions are exposed to different temperatures One of these is maintained at a constant temperature level while the other is applied to the skin Each is composed of one or more junctions of two dissimilar metals having different coefficients of expansion The galvanometer is calibrated in degrees Centigrade or Fahrenheit or both

A simpler and much less expensive method for recording skin temperature is the use of a modified mercury thermometer with a flat widened base The latter is held firmly against the skin and the level is read off on the scale recording the height of the mercury column However there are a number of objections to its use First the thermometer is fairly insensitive with the result that the bulb portion has to be held in contact with the skin for some time before the complete change is recorded This introduces an artifact since prolonged pressure may cause emptying of cutaneous capillaries and hence a decrease in loss of heat beneath the thermometer Furthermore the instrument may interfere with normal evaporation of sweat from the skin and thus alter its temperature If a gross approximation of the change in cutaneous temperature is all that is desired this type of apparatus will suffice However if accurate and reproducible results are required then an instrument utilizing thermocouples is necessary

Steps for Determining Changes Produced by Elimination of Vasomotor Tonus Before vasomotor tonus is *removed* it is necessary first to obtain control skin temperature readings The patient rests on a bed with the extremities to be studied exposed to the room temperature while all external stimuli are reduced to a minimum After allowing approximately 20 minutes to pass for stabilization of the cutaneous temperature readings are taken from the following sites ventral surface of all the digits several locations on the dorsum of the hand or foot and one or two on the forearm or leg Once constant figures are noted vasomotor tonus is temporarily eliminated by one of the methods listed below and another set of determinations is made

PROCEDURES USED CLINICALLY FOR TEMPORARY REMOVAL OF VASOMOTOR TONUS

Procaine Block of Peripheral Nerves Clear-cut but limited information as to the degree of existing vasospasm can be obtained by injecting a local anesthetic around the peripheral mixed nerves in the limbs Generally 1% procaine solution provides an adequate block

In the lower extremity, partial sympathetic denervation is obtained through anesthetization of the posterior tibial nerve The medial aspect of the foot is prepared surgically and draped with sterile towels and then 3 cc of the procaine solution is injected into the tissues behind and below the medial malleolus, in the vicinity of the posterior tibial artery At times the nerve can be felt as a cord like structure in this site, digital compression producing a tingling sensation in the toes A successful block is manifested by the appearance of anesthesia of the plantar surface of the digits, particularly the great toe, anhidrosis, and a pink color Such findings should be noted within 10 to 15 minutes after the injection of the anesthetic If no appreciable change occurs at the end of this period the procedure should be repeated After the expected changes are present, skin temperature readings of the digits and dorsum of the foot are recorded at 10 to 15 minute intervals until no further elevation is obtained

In the upper extremity, the desired effect is produced by anesthetization of the ulnar nerve at the elbow and the median nerve at the wrist When both structures have been properly blocked, anesthesia of the palmar surface of all five fingers results, together with inhibition of neural vasomotor control of the cutaneous vessels in these areas The rise in skin temperature readings of the hand and forearm is then recorded

Blocking of Sympathetic Ganglia or Trunks Blocking of appropriate paravertebral sympathetic ganglia or of sympathetic trunks through spinal anesthesia will also cause sympathetic denervation of the extremities However, in contrast with the preceding method these are hospital procedures and hence the description of their technic will not be presented A detailed discussion of such procedures can be found in monographs on regional block[1, 2] (For physiologic changes produced by blocking the sympathetic nervous system, see Chap XXVII)

Indirect Vasodilatation (Reflex Vasodilatation) A method of removal of sympathetic tone which can be performed in the office the clinic or at the bedside is by the use of heat to various parts of the body, excluding the limbs under study A number of different measures can be utilized, such as the application of 4 or 5 hot water bottles or several electric pads to the axillae abdomen and chest while the trunk is covered with heavy blankets A heat cradle heat lamp or diathermy can be substituted as a source of heat Another procedure consists of the immersion of the limbs not being studied in buckets containing water at a temperature of 45° C (113° F) This level is maintained for approximately one hour by the addition of hot water when required No heat is applied to the trunk although it is covered with blankets One precaution that must be borne in mind with this method is that only limbs with a normal arterial circulation should be exposed to the hot water (For the physiologic basis of this test, see *Body Heating Producing Indirect or Reflex Vasodilatation* Chap XXVIII)

The most obvious change elicited by body heating is sweating * This generally begins about one half hour after application of the heat, at which time another set of skin temperature readings is obtained The procedure is then repeated at half hour intervals until the maximal rise in surface temperature is reached This

* Since this is usually considerable it is advisable to have the patient disrobe and put on a hospital gown before the test is started

usually takes place one and one half hours after onset of sweating It is necessary to point out however that vasodilatation is produced more slowly in the toes than in the fingers and hence it is necessary to prolong the procedure if the anticipated rise in skin temperature in the feet does not occur within this period It is preferable to warn the patient that he must expect to become rather uncomfortable toward the end of the examination The application of the heat is enervating and the loss of salt in the perspiration contributes to the feeling of weakness Generally all symptoms disappear within several minutes after the test is terminated If the subject is ambulatory it is better to have him remain indoors for 10 or 15 minutes after dressing in order to allow his body to cool off slowly

CHANGES IN CUTANEOUS TEMPERATURE FOLLOWING TEMPORARY SYMPATHETIC DENERVATION

Normal Subjects After removal of sympathetic control by any one of the methods already discussed the readings in the hands and feet of normal individuals should rise to at least 30° C (86 F) and generally to between 31° and 35° C (88 and 95° F) The figures may be about 2° higher with blocking of nerves or ganglia than with indirect vasodilatation probably because the anhidrosis which follows anesthetization of sympathetic fibers eliminates the cooling ordinarily produced by the evaporation of perspiration

Patients with Vasospasm In the case of the subject manifesting excessive sympathetic activity in the vessels of the extremities inhibition of vasomotor tonus will cause a change from low control readings (similar to or even below room temperature) to 31-35° C (88 to 95° F) The latter are similar to those obtained in normal individuals but the magnitude of the increase is much greater because the control figures are lower The difference between the two sets of readings therefore can be considered a gross index of the degree of vasomotor control existing initially

Patients with Structural Changes In the subject with an obliterative vascular disease alone removal of vasomotor tonus generally results in a rise from around 24° or 25 C (75 or 77 F) to 27 or 28 C (80° or 82° F) but not higher In other words in spite of elimination of all sympathetic influence the normal increase in arterial inflow does not occur because structural changes in the cutaneous vessels prevent adequate dilatation Frequently some vasospasm exists in conjunction with the organic process as in thromboangiitis obliterans and under these circumstances there is an increase from a low control reading to about 29° C (84° F) Temperature levels of 26° C (79° F) or less after successful sympathetic denervation indicate a severe degree of an occlusive arterial vascular disease Removal of vasomotor tonus may in some instances be followed by an actual drop in surface temperature of one or more toes This apparently paradoxical type of response has great significance since it eliminates the use of sympathectomy as a therapeutic procedure (p 450)

COMPARATIVE VALUES OF DIFFERENT PROCEDURES

Advantages and Disadvantages of Each Test The choice of a method for the removal of vasomotor tonus is frequently determined by what information beyond

that relating to vascular patency and tonicity is desired. In favor of such procedures as peripheral nerve block and indirect vasodilatation is the fact that hospitalization is not required in their performance. However, they, as well as spinal anesthesia, give no information as to whether sympathetic denervation would be of value for the treatment of pain of vascular origin. The only procedure of use in this regard is paravertebral sympathetic block, since it produces paralysis of sympathetic fibers without affecting sensory pathways. Another disadvantage in the use of indirect vasodilatation is the fact that the procedure may not be effective in producing complete sympathetic denervation in cases of severe vasospasm unless heating is prolonged. The other methods are not open to this criticism, provided the examiner is certain that full anesthetization of the nerve or ganglia has occurred. Not infrequently, in the case of paravertebral block or nerve block, if the anesthetic has been inadvertently injected some distance from the nervous structure, the amount of material that eventually reaches it by diffusion may be insufficient to cause complete anesthesia. This possibility does not hold for spinal anesthesia, for once the anesthetic enters the spinal canal there is little doubt that the nerves will be exposed to its full action.

Spinal anesthesia is generally utilized if a lumbar sympathectomy is contemplated. If the results of the test indicate that this procedure might be of some therapeutic use, as suggested by a significant rise in cutaneous temperature, then the operation can be carried out while the patient is still in the stage of surgical anesthesia from the spinal injection. Another advantage of this approach is that a comparison is possible between responses in the two feet. This may be sufficiently clear-cut to indicate which extremity has the more advanced occlusive arterial vascular process and will therefore perhaps be the first to show nutritional disturbances.

Certain criticisms and limitations apply to all the above procedures. First, it must be noted that the skin temperature alterations produced by removal of vasomotor tonus are merely qualitative and indirect indices of variations in cutaneous circulation. They give no information concerning the local blood flow to deeper tissues of the extremities. In this regard it is generally accepted that a pathologic process can exist in the muscle vessels with those in the skin remaining unaffected, and vice versa. Furthermore, even when used to determine the state of the cutaneous blood supply, the tests do not distinguish between a response elicited in a normal vascular tree and one in which structural alterations have occurred at such a slow rate that there has been sufficient time for the formation of an adequate collateral circulation.

It must also be borne in mind that the usual sites for study of cutaneous temperature, the digits, contain a specialized type of vessel, the arteriovenous shunt, whose reaction to various stimuli is marked (p. 412). Hence information thus obtained can not be interpreted as representative of circulatory responses elsewhere in the cutaneous vascular bed.

Summary. The various procedures which temporarily remove sympathetic control over blood vessels in the extremities are of value in obtaining information regarding the degree of vasomotor tonus in the cutaneous arterial tree in the digits and in determining whether or not vasospasm exists. They are also helpful in

diagnosing an early occlusive arterial vascular disease and in estimating the degree of structural involvement present Peripheral nerve blocking and indirect vasodilatation are office and bedside procedures, while paravertebral sympathetic blocks and spinal anesthesia can only be performed in the hospital Since all these tests also give information concerning the capacity for vasodilatation they are useful in arriving at a decision as to whether or not such a procedure as sympathectomy is indicated as a therapeutic measure However it must be emphasized that they are of little or no value in determining the state of the circulation in the muscles

TESTS FOR DETERMINATION OF STATE OF MUSCLE CIRCULATION

Unfortunately no objective simple clinical test exists for the full evaluation of the circulation in the muscles of the extremities It is therefore necessary to resort to the subjective response of the patient to a standard exercise to obtain a qualitative estimate of the degree of involvement in this vascular bed For clinical purposes such a measure is adequate provided the patient's word can be trusted and no ulterior motive exists to cause him to exaggerate or falsify symptoms If it is desired to gauge the efficacy of a therapeutic agent for increasing muscle blood flow care must be taken to substitute placebos in the course of the treatment in order to determine whether or not an actual causal relationship exists between whatever subjective improvement occurs and the administration of the medication At the same time all other conditions must remain constant

CLAUDICATION TIME AND DISTANCE

The simplest test for determination of the efficiency of muscle circulation is the measurement of the ability of the patient to walk before experiencing symptoms in the exercising muscles The greater the arterial impairment the shorter the distance covered or the time before pain is experienced It is necessary to set the pace by walking with the subject at a rate of 100 to 120 steps per minute on a level surface and to determine with a stop watch the exact time of the initial appearance of symptoms in the muscles (*claudication time*) and the interval until the patient is compelled to stop The data can also be recorded as the length of the walk expressed in standard sized city blocks (*claudication distance*) Although utilizing information obtained from the clinical history of the patient may be open to criticism if used in an experimental study such a source is probably adequate for the diagnosis of an impaired muscle circulation and for determination of the extent of involvement (For the physiologic basis of this test see *Intermittent Claudication* Chap XXVIII)

A modification which perhaps gives some degree of objectivity to the above test is the performance of oscillometric studies before and immediately after physical activity Normally with walking there is a local dilatation of the medium sized and small arteries supplying the exercising muscles and this is reflected as an increase in the swing of the oscillometer needle In patients with structural altera

tions in the vessels, no significant change in the figures is noted under these circumstances However, it must be borne in mind that in some instances exercise may produce spasm of apparently normal arteries, and that this response will then be manifested by a reduction in oscillometric readings

Summary The available clinical tests for the determination of the degree of impairment of muscle circulation, for the most part, are not particularly satisfactory Aside from the information derived from eliciting a careful history of pain in the muscles of the lower extremities on walking a specific distance or for a certain period of time the others are laboratory or hospital procedures and hence not applicable to the routine office vascular examination

REFERENCES

1 Moore D C *Regional Block Handbook for Use in Clinical Practice of Medicine and Surgery* Springfield Ill Thomas 1953
2 Moore D C *Stellate Ganglion Block* Springfield Ill Thomas 1954

CHAPTER

V PROCEDURES FOR STUDY OF VENOUS CIRCULATION IN THE EXTREMITIES

Careful examination of the veins in the extremities is an essential part of a vascular survey particularly since in clinical practice disorders of this portion of the circulation are generally much more prevalent than those affecting the arteries and their branches The tests can be divided into two types one determines the status of the superficial veins and the other the condition of the deep veins Some are useful for the study of both systems A summary of these tests will be found in Table 6 p 66

EXAMINATION OF THE SUPERFICIAL VENOUS SYSTEM

INSPECTION AND PALPATION

Inspection and palpation of the skin and subcutaneous tissues of the limb may elicit considerable information concerning the state of the superficial veins These vessels should be examined for evidence of thrombosis inflammation abnormal prominence distension pulsations and regurgitant flow

Thrombosis of Superficial Veins

Characteristics of Lesion Red streaks in the skin about one half inch in width and of varying lengths may indicate the presence of thrombosed superficial veins with an associated phlebitis and periphlebitis (Fig 30 p 235) Such an impression is confirmed by palpating the site and determining the existence of an increase in cutaneous temperature directly over and in the vicinity of the lesion and of a cordlike mass beneath the skin In order to differentiate a thrombosed vein from a dilated one it is necessary to outline the entire length of the involved segment on the skin and then elevate the limb Under these circumstances a prominent vessel will collapse and become imperceptible to the examining finger while a thrombosed vein will remain unchanged However it is necessary to point out that a distended vessel due to an increased venous pressure or one with venofibrosis may likewise be unaffected by the maneuver although in neither instance is a mass felt

Location of Lesion The most likely sites for benign superficial thrombophlebitis are along the course of the two main superficial venous systems In the case of the great saphenous vein the medial aspect of the thigh should be inspected while for the small saphenous vein, attention should be directed to the lateral and posterolateral surfaces of the leg up to the level of the popliteal space All clusters of varicose veins warrant careful examination, since these have a tendency to thrombose spontaneously or the process may have been initiated by the use of therapeutic sclerosing solutions In thrombophlebitis migrans the involved veins may be located practically anywhere in the four extremities but more often in the lower limbs (Fig 31 p 238)

Dilated and Prominent Superficial Venous Channels

The extremities should always be examined for the presence of distended and prominent superficial veins Since the latter may not always be noticed with the limb in the horizontal position it is necessary to make a routine procedure of having every patient stand on a stool, so that the hydrostatic effect of the column of blood will dilate and bring the veins into view In contrast to varicosities the venous valves in distended or prominent veins are still competent and hence there is no backward or regurgitant flow (For visualization of superficial veins see *Infrared Photography*, Chap XXV)

Dilated or Prominent Veins in Normal Subjects Large distended veins may be present normally in thin persons particularly if they have lost weight rapidly The subcutaneous tissue ordinarily supplies an element of support for such vessels and if this is reduced in amount the veins tend to become dilated Prominence of small thin walled superficial veins may also be a normal finding especially in obese females These structures are generally seen on the lateral aspect of the thighs in the popliteal space and in the region of the malleoli They may become more apparent during pregnancy and remain unchanged after delivery Aside from the effect on the esthetic sensibilities of the patient they have no significance

Congenital Abnormalities in Superficial Venous System A marked prominence and diffuse dilatation of the subpapillary venous plexus may produce a similar picture to the above except that generally the alterations are more extensive and are not limited to the limbs Such a finding has little clinical significance Since the thin walled vessels are very close to the surface and hence vulnerable to trauma, there may be associated ecchymosis but rarely bleeding

Phlebectasia another congenital anomaly is characterized by enlargement and fusiform dilatation of the superficial venous channels in the limbs (Fig 61 p 375) It may be mistaken for the distended venous network observed in conjunction with congenital arteriovenous fistula (For further discussion see *Phlebectasia*, Chap XXIII)

Occlusion of Main Venous Channel in Extremity Distended veins may be a prominent finding in the early stage of thrombosis of the main deep vein in an extremity The abnormality is due to the shunting of blood from the deep into the superficial venous system in an attempt to bypass the blocked portion of

vessel This produces an increa e in venous pressure and *dilatation of the* chan nels *Frequently* however the change is masked by the associated pitting edema and only becomes apparent when the latter *disappears* The distended veins may remain for some time after the acute stage has subsided

As a sequel of deep *thrombophlebitis the superficial* venous network in the limbs may become conspicuous The increase in the size of this vascular bed *represents* in part the formation of a collateral system to take over the function of returning blood to the heart from *the extremity* In the case of *iliofemoral* thrombophlebitis the new network is gener ally *noted on* the lateral aspect of the thigh the flanks and the lateral and anterior portions of the abdominal wall (Fig 4) Following axillary vein thrombosis a similar type of change may be present on the upper part of the arm and the adjoining half of the *anterior* chest wall (Fig 3, A p 60)

Extrinsic Pressure on or Obstruction of Main Venous Channels Proximal to Extremity The sudd n and apparently spontaneous appea ance of dilated superficial veins in the limbs may *indicate* the presence of some ex trinsic obstruction to venous outflo as for example a tumor in the *pelvis or a gravid uterus* Occlusion of the superior or inferior vena cava is associated with the presence of large d stended and tortuous *superficial* veins not only *in the* limbs but also on the anterior *surface* of the chest and abdomen (Fig 66 p 39-) The extent *and ramifications* of these vessels are made apparent by having the patient raise his intrathoracic pressure through the Valsalva maneuver



Fig 4 Extensive network of superficial venous collateral vessels on thigh and abdomen following l ft iliofemoral thrombophlebitis (infrared photography)

Communication between Vein and Artery *Dilated* enlarged superficial veins may be present when *a traumatic* arteriovenous aneurysm exists in the extremity Under such circumstances the blood flow through these vessels is markedly *increased and* venous pressure approaches that in the *arterial system In fact* pulsations can at times be seen *and felt in some* of the veins An indication *of the* high pressure is obtained by elevating the limb above the level of the heart Ordinarily the veins will collapse in this position but in the presence *of an* arteriovenous aneurysm they remain *distended* To confirm the *diagnosis* other *signs of* an abnormal communication between artery and vein should be sought (See *Clinical Characteristics of* arteriovenous *aneurysms*, Chap XVII)

Phlebosclerosis Veins which appear dilated in the horizontal and elevated positions must be differentiated from those with phlebosclerosis (*venofibrosis*)

In the latter condition the vessels are prominent, not as a result of distension by blood, but because the walls have lost their normal *elasticity and collapsibility*

Procedures for Determining Competency of Valves in Superficial and Communicating Veins

Since inspection and palpation alone are frequently not sufficient to differentiate between varicose and dilated veins, it is necessary to resort to several tests to make this distinction Their purpose is to give information regarding sites of incompetency in the great and small saphenous veins and in the communicating vessels which connect the superficial and deep venous networks at various levels in the thigh and leg Since failure to treat incompetent communicating veins surgically may be a primary cause of recurrence of varicosities,[2] it is essential preoperatively to locate accurately all such vessels

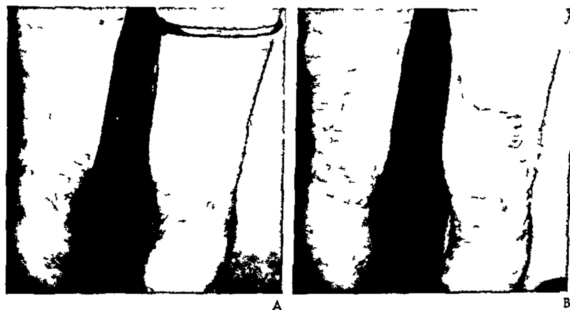


Fig 5 Demonstration of incompetency in the great saphenous vein at the level of the saphenofemoral junction using the Trendelenburg test A Tourniquet applied high on the thigh while patient was lying down and extremity was elevated On standing no varicosities noted B Tourniquet removed with immediate appearance of varicosities on posterior aspect of thigh and leg (From D I Abramson Practical procedures in bedside diagnosis of peripheral vascular disorders *General Practitioner* 6 546 1955)

Brodie Trendelenburg Test

Technic The Brodie Trendelenburg test (commonly known by the latter name alone) besides differentiating between dilated and varicose superficial veins of the lower extremity, is also of value in determining whether or not incompetent communicating veins are present The procedure is performed as follows The patient lies down and the limb is elevated to empty the superficial veins While the patient is in this position a rubber tourniquet is applied around the thigh just below the level of the fossa ovalis The degree of compression utilized is much less than that which would obstruct arterial inflow or movement of blood

out of the femoral vein but is sufficient to collapse the great saphenous vein The patient now stands with the portion of the leg displaying the varicosities facing a good light and within 10 seconds the tourniquet is released An immediate filling of the great saphenous vein and its tributaries from above downward implies that the valves in the main vessel are incompetent probably at the level of the fossa ovalis and that blood is leaking backward into the superficial venous system through the saphenofemoral junction (Fig 5) * A slow filling of the vessels (30 seconds or more) is a normal response being due to the upward movement of blood from the capillary system If instead of removing the tourniquet almost immediately the compression is maintained further pertinent information can be obtained The rapid appearance of dilated vessels in one or more areas below the level of the constricting band indicates that there has been a *reflux flow* into them either from the small saphenous vein or from incompetent communicating branches

There has been some confusion concerning the proper manner of recording the results obtained with the above procedure Such terms as a negative or a positive Trendelenburg test should be discarded since they are ambiguous and misleading *For the sake of clarity* it is much better to express all changes as indicating competency or incompetency of the valves in question

Multiple Tourniquet Test

The multiple tourniquet test a modification of the Trendelenburg test is performed as follows With the extremity elevated four tourniquets are applied three to the thigh so as to compress the upper middle and lower segments respectively and one to the leg just below the knee[9] The patient now stands and the rate of filling of the superficial veins is noted If this occurs rapidly with all four bands in place (*i e* in less than 30 seconds) it can be assumed that there are incompetent communicating veins in the leg below the level of the fourth tourniquet If no change is noted the latter band is removed Immediate filling of the superficial veins implies that the small saphenous vein is incompetent The same type of response resulting from removal of the tourniquets just above the knee and around the middle of the thigh indicates that the involvement is in veins other than the great saphenous Finally sudden distension of veins on the leg and thigh on release of the last tourniquet localizes the difficulty to the saphenofemoral junction Therefore by means of the multiple tourniquet test the site or sites as well as the existence of incompetency in the superficial and communicating veins can be determined

Thumb-Compression Tourniquet Test

In the study of the small saphenous vein it is advisable to supplement the data obtained with the Trendelenburg or the multiple tourniquet test by the use of digital pressure applied to the popliteal space[1 3]

The leg is elevated to empty the veins and a tourniquet is placed around the

* The small saphenous vein can be tested in a similar manner using a tourniquet applied just below the level of the popliteal space

lower part of the thigh to prevent any regurgitation of blood through the great saphenous system The popliteal space is now compressed with the thumb the remaining fingers taking a firm grip on the anterior aspect of the knee for stabilization of the pressure The patient is allowed to stand while the compression is maintained for 20 to 30 seconds Absence of sudden filling of the veins in the lower part of the leg can be considered a normal response However, if these vessels almost immediately become distended despite the continued application of a digital pressure it can be assumed that the site of reflux is in the communicating veins joining them If filling occurs from above downward only after removal of pressure in the popliteal space, it indicates that the incompetency is in the small saphenous vein The Trendelenburg or the multiple tourniquet test alone does not as readily differentiate between involvement of the communicating vessels and of the small saphenous vein

Pratt Test

Another test which gives information regarding the state of the valves in the communicating veins is performed as follows With the leg elevated a tourniquet is placed high on the thigh and an elastic bandage is applied, beginning at the toes and ending at the groin [7] The patient then stands and the bandage is slowly unrolled from the top down while the tourniquet is still maintained to prevent a leak at the saphenofemoral junction Any incompetency in the valves of a communicating vessel will reveal itself by the sudden appearance of a collection of distended veins at the level at which the bandage is being unwound As a confirmatory measure the vessels are collapsed by digital pressure and then the finger is removed The immediate reappearance of the dilated veins is further proof for the diagnosis Once an incompetency is found it is necessary to repeat the test except that the tourniquet is now placed around the limb just below the level at which distended vessels were previously noted Such a step prevents filling of vessels distally by regurgitation of blood from above As each group of incompetent veins is identified it is marked off

Percussion (Schwarz) Test

If a varicose vein is distended by blood as on standing and is then tapped with a finger a disturbance is initiated which travels in either direction in the form of a wave along the fluid column This can be felt as an impulse some distance from the site of origin although marked obesity or extreme tortuosity of the vessels may at times damp the effect In a vein with competent valves proximal spread occurs only to a minor degree while distal spread is not obtained at all Such differences are due to the fact that in the upright position a normal vein contains much less blood than a varicose vein with the result that there is poorer propagation of the wave

The technic of the percussion test is as follows The fingers of one hand are placed over the great saphenous vein at the fossa ovalis while those of the other apply an abrupt thrusting blow to a dilated segment of vein in the leg If the upper digits pick up a definite and strong impulse then the procedure is reversed If per

cussion of the vein at the fossa ovalis now produces a wave which travels down to the fingers below this is strong evidence that the valves are incompetent The same type of procedure can be applied to the small saphenous system

EXAMINATION OF THE DEEP VENOUS SYSTEM

INSPECTION AND PALPATION

Because of their location deep in the tissues the main venous channels in the extremities do not lend themselves to inspection and palpation Still such means are useful in obtaining information indirectly regarding these vessels particularly if sudden occlusion occurs Under these circumstances obvious changes will be noted in the superficial venous system and on the surface of the limb such as pitting edema distended superficial veins and cyanosis and coldness of the skin Hence no difficulty should be encountered in making the diagnosis at this stage Later sequelae of the condition appear such as swelling pigmentation of the skin and ulceration However it must be pointed out that such findings are no different from those which result from venous stasis due to primary varicosities except that they are generally more marked

PROCEDURES FOR THE DETERMINATION OF THROMBOSIS OF THE DEEP VEINS OF THE CALF AND FOOT

One of the most difficult clinical entities to recognize in the field of peripheral vascular disorders is a bland thrombus in the deep venous system of the calf and foot Nevertheless because of the gravity of its main complication pulmonary embolism every effort should be made to determine its early presence Patients who are potential candidates for intravascular clotting particularly should be frequently and carefully examined with the possibility of deep vein thrombosis in mind For this purpose several tests are available

Homans Sign

The most popular procedure is the one described by Homans[4] This consists of lifting the leg from the bed with one hand and forcibly dorsiflexing the foot so as to place the tissues comprising the posterior portion of the calf under stretch If the deep veins in this site are *thrombosed* these structures now firm will cause pressure on the adjoining mixed nerves to produce pain locally The effect of the movement is enhanced because the loose connective tissue which ordinarily surrounds veins and acts as a buffer to reduce pressure on [illegible] the calf Some [illegible] the sole [illegible] dorsiflexi[illegible] a positive [illegible] in the foot may indicate that there are thrombi in the plantar veins which may also act as a source for readily dislodged clots

In the interpretation of the response in the calf it is important to point out that much too frequently a false positive test is obtained which may result in needless surgery This is because any type of inflammation in the vicinity of the

lower part of the thigh to prevent any regurgitation of blood *through the great* saphenous system The popliteal space is now compressed with the thumb, the remaining fingers taking a firm grip on the anterior aspect of the knee for stabilization of the pressure The patient is allowed to stand while the compression is maintained for 20 to 30 seconds Absence of sudden filling of the veins in the lower part of the leg can be considered a normal response However, if these vessels almost immediately become distended, despite the continued application of a digital pressure, it can be assumed that the site of reflux is in the communicating *veins joining them If filling occurs from* above downward only after removal of pressure in the popliteal space, it indicates that the incompetency is in the small saphenous vein The Trendelenburg or the multiple tourniquet test alone does not as readily differentiate between involvement of the communicating vessels and *of the small saphenous* vein

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be obtained regarding the site of incompetency Finally, if the deep veins are not patent or if there is an increased pressure in them the superficial vessels will become more distended during the period of exercise

Elevation of Limb

A test for patency of the deep venous system consists of applying a tourniquet to the thigh while the patient stands so as to distend the veins with blood Then he lies down and elevates his extremity The compression is continued in order to prevent blood from leaving the limb through the great saphenous system If the superficial vessels remain dilated despite elevation of the extremity, it can be assumed that a block exists in the deep venous system[6] If such a state is not present the superficial veins will collapse as blood drains from them into the deep veins via communicating channels, and then out of the extremity However since the possibility exists that the blood may still be pooled in the deep venous system rather than having left the limb it is necessary to carry out another step The patient stands again with the tourniquet still on if the superficial veins now suddenly distend the initial response can not be considered to indicate patency of the deep veins

Elastic Bandage Test

Information regarding the efficiency and patency of the deep venous circulation can be obtained by the use of the elastic bandage test The extremity is elevated in order to collapse the superficial veins and while in this position careful measurements are made of the circumferences of the leg Then it is wrapped in a snug elastic bandage beginning with the toes and extending up to the knee and the patient is instructed to walk at an average pace for approximately one half hour At the end of this period a second group of measurements of calf size is obtained with the limb elevated

In the presence of a block in the deep venous system definite discomfort will be experienced during physical effort becoming progressively worse as the exercise is prolonged On removal of the bandage the symptoms are instantly relieved Under such circumstances an increase in the size of the calf will generally be noted at the termination of the walk this finding having the same significance as the pain

If the deep veins are patent and the communicating channels are competent the use of the bandage during exercise should be associated with no complaints In fact the patient generally derives some benefit from this procedure since the compression collapses the superficial varicose veins and shunts the blood into the deep vessels through the perforating branches (For technic of and indications for venography see Chap XXV)

Determination of Venous Pressure in the Upper Extremities

calf may cause pain when the involved tissues are placed on stretch by Homans maneuver (For further discussion of this point see *Differential Diagnosis of Phlebothrombosis*, Chap XIV)

Other Signs

A number of other tests, not as well known as Homans sign, can be utilized in clarifying this problem One of these consists of palpating for an area of infiltration in the general region of the deep veins of the calf [6] This is performed by having the patient rest his heels on the bed, flex the knees, and relax the calf muscles Thickening and infiltration deep in the gastrocnemius muscle and tenderness are considered a positive sign This finding may exist in venous thrombosis even when Homans sign is negative

A test which may be of value in determining whether there are pathologic changes *in the deep veins of the anterior muscles of the leg is performed as follows* The foot is passively extended 45 degrees or less and, if this elicits no pain the toes are plantar flexed as the foot is held in extension [8] The sign is positive and reveals evidence of thrombosis of the anterior tibial vein if the maneuver elicits pain anywhere just lateral to the anterior crest of the tibia, but especially at the point three inches above its distal end In the latter location this vessel is most superficial in its course and hence contraction of the anterior group of muscles, brought into play by extension of the foot can readily cause its compression Clinically, the possibility of involvement of the deep veins of the anterior muscles of the leg has not been considered seriously and it may be that by the use of this sign there will be a reduction in the number of cases of so-called 'silent venous thrombosis [8]

Tests for Determining Patency and Competency of the Deep Venous System

Thrombosis of a main deep venous channel may result in either permanent *occlusion or recanalization with destruction of the valves locally the latter producing a patent but incompetent vessel* Because the prognosis may be different it is necessary to determine in each case of postphlebitic syndrome which situation exists Information concerning the state of the deep venous system is also mandatory when ligation and excision of superficial veins are contemplated Several tests which are of value in this regard are presented below Some of these are similar to those already described except for minor modifications

Perthes Test

The subject stands, and after a tourniquet is placed around the thigh to compress the great saphenous vein he either alternately flexes and extends the knee about 10 times or walks If the deep veins are patent and competent the exercise will cause the blood to flow into them with the result that the superficial vessels will collapse and remain so If the deep veins are patent but incompetent the superficial veins will empty during the physical effort but will then refill as soon as this is terminated By applying the tourniquet at different levels information can

level to which the blood rises in the tube is read off in centimeters or millimeters A reading between 60 and 120 mm of water (4.4–8.8 mm Hg) is considered normal The test can be repeated several times by allowing the mixture of saline and blood in the tube to be withdrawn by means of the syringe and then connecting the needle with the tube again to determine the new height of the column of liquid The preliminary filling of the tube with saline solution may help decrease the entrance of blood into the cylinder and thus minimize the tendency to clotting

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Table 6 Outline of Peripheral Vascular Examination

Arterial circulation

Inspection and Palpation

Skin color in horizontal elevated and dependent positions hyperhidrosis trophic changes edema (pitting and lymphedema) changes in texture of skin pigmentation of skin

Tests for Cutaneous Circulation
Plantar pallor test subpapillary venous plexus filling time histamine wheal test reactive hyperemia test

Examination of Peripheral Arteries
Pulsations in radial, ulnar femoral popliteal posterior tibial and dorsalis pedis arteries designated as 0 1 2 3 or 4+ presence of aberrant arteries ulnar confirmatory test *venous filling time oscillometric* readings at thigh above knee calf and leg above ankle

Venous circulation

Inspection and Palpation
Dilated and prominent veins thrombosed superficial veins signs of venous stasis (edema pigmentation stasis dermatitis stasis ulceration brawny induration of skin)

Tests for Competency of Valves in Superficial Veins
Trendelenburg test multiple tourniquet test Pratt test percussion test

Tests for State of Deep Veins
Homans sign Neuhof's sign Perthes test elastic bandage test venous pressure determination

to the level at which the reading is being *obtained* The procedure *does not* however distinguish between extrinsic compression of the vessel and obstruction of the lumen by a thrombus Nor does it differentiate between a local mechanism causing a rise in pressure and one due to some systemic condition such as congestive heart disease, pericarditis with effusion or constrictive pericarditis The *technic used for the upper extremities* is as follows*

A #18 needle is attached by means of a three way stopcock to a vertical glass cylinder, graduated in millimeters The apparatus is wetted with a small quantity of concentrated citrate solution and the glass tube is partly filled with sterile isotonic saline *solution from a syringe attached to another end of the stopcock* The needle is inserted into one of the large veins at the cubital fossa the limb having been placed at approximately the level of the right atrium This is accomplished by having the patient lie flat on his back with his arm resting on a pillow so that the cubital fossa is situated about two thirds of the distance from the back to the level of the anterior surface of the sternum

When there is a free flow of blood through the needle into a syringe attached to the stopcock, the needle is now connected to the vertical glass cylinder and the

* A crude indication of venous pressure can be obtained by noting the degree of elevation of the arm necessary *to produce collapse of the veins on the dorsum* of the hand If only one extremity is involved the other can be used as a control The same measure can be applied to the leg (For technic of and indications for venous pressure measurements in the lower extremities see Chap XXV)

litis Finally, it may be found as part of the clinical picture of atrophy of disuse from prolonged immobility of an extremity (For a summary of the various conditions in which vasospasm is found see Table 12 Chap VIII)

ABNORMAL NEUROLOGIC SIGNS

Since irritation of peripheral nerves may follow impairment of local arterial blood supply or be induced by the same factor responsible for the circulatory disturbance it is essential in many instances to supplement the vascular examination by a simple neurologic study The digits and the rest of the extremity should be tested for vibratory sense perception response to pin prick and cotton wool deep reflexes and on occasion identification of cold and warmth (Table 7)

VASCULAR DISORDERS MANIFESTING ABNORMAL NEUROLOGIC FINDINGS

Chronic Anoxia Chronic arterial insufficiency may eventually produce enough persistent anoxia of the peripheral nerves through impairment of blood flow in nutrient vessels to these structures to initiate a mild to moderate degree of ischemic neuritis In arteriosclerosis obliterans the terminal portions of the nerves may actually demonstrate wallerian degeneration and perineural and intraneural fibrosis Somewhat similar changes may be noted in long standing thromboangiitis obliterans Objectively, however the degree of involvement of peripheral nerves in these two conditions is generally minimal consisting of slight impairment in vibratory sense perception and response to pin prick When the individual with arteriosclerosis obliterans also has diabetes it may be difficult to determine whether the neurologic findings are due to the anoxia of nerves associated with an impaired circulation to the diabetic state or to both factors Another chronic occlusive vascular disorder which manifests neurologic changes in the extremities is polyarteritis nodosa These may take the form of a typical polyneuritis with involvement of any of the peripheral nerves (For discussion of symptoms see Ischemic Neuritis Chap I)

Acute Anoxia Sudden and complete occlusion of the blood supply to an extremity as in arterial embolism or thrombosis is invariably accompanied by marked changes in the peripheral nerves As a result of the acute and persistent anoxia of all segments of the nervous elements below a certain level on the involved extremity a stocking glove type of anesthesia or hypesthesia occurs This is generally accompanied by loss of voluntary movements of the digits and adjoining portion of the extremity as well as foot drop and less frequently wrist drop Usually no sensation is experienced in the digits

Pressure on Nerves Syndromes in which the circulatory disturbance is due to compression of the subclavian artery or vein are almost invariably associated with concomitant pressure on the brachial plexus producing neurologic findings in the limb Into this category fall such clinical entities as the cervical rib the scalenus anticus the costoclavicular and the hyperabduction syndromes The neurologic manifestations may be hypesthesia hyperesthesia and slight weakness or even paralysis of the muscles with atrophy of varying degree

CHAPTER

VI DIFFERENTIAL DIAGNOSIS OF PHYSICAL FINDINGS

I EXCESSIVE SYMPATHETIC TONUS, ABNORMAL NEUROLOGIC SIGNS, ENTITIES ASSOCIATED WITH PETECHIAE AND ECCHYMOSIS, CUTANEOUS AND SUBCUTANEOUS MASSES, SWELLING

This and the following chapter will deal with a differentiation of those abnormal findings commonly present in an extremity suffering from a vascular disease No attempt will be made to present a complete discussion of the particular circulatory disorders considered in the text, since such detailed information can be obtained by reference to the second part of this volume

EXCESSIVE SYMPATHETIC TONUS

A cold cyanotic or pale moist extremity with or without swelling indicates the presence of excessive sympathetic tonus Regardless of the etiology the manifestations are always the same They result from a greater than normal degree of sympathetic stimulation of sweat glands and cutaneous blood vessels, especially those in the distal portion of the limb (For further discussion of this subject see *Vasospasm* Chap XXVII)

Vasospasm may be present in a number of different disorders vascular and non vascular *In certain functional circulatory states* it dominates the clinical picture as for example in Raynaud s disease Raynaud s syndrome acrocyanosis livedo *reticularis posttraumatic vasomotor disorders and causalgic states* Entities which follow exposure to extreme cold or dampness such as frostbite trench foot and immersion *foot likewise demonstrate signs of hypertonus but to a lesser degree* This state may be present in conjunction with such organic vascular diseases as thromboangiitis obliterans, *the acute stage of arterial embolism acute deep* thrombophlebitis and the postphlebitic syndrome Examples of nonvascular dis orders in which vasospasm exists are rheumatoid arthritis and *anterior poliomye*

Table 7 Differential Diagnosis of Neurologic Abnormalities in the Extremities

Clinical entities in which changes are found	*Etiologic factor or pathogenesis*	*Predominant symptoms*	*Predominant neurologic signs*	*Signs of arterial impairment*
Arteriosclerosis obliterans thrombo angiitis obliterans polyarteritis *nodosa*	Chronic ischemic neuritis	Rest *pain* lancinating in character paresthesia burning sensation sense of coldness	Mild loss of vibratory sense hypesthesia transient foot & wrist drop *in* polyarteritis nodosa	Invariably present in a o & t a o absent or slight in polyarteritis nodosa
Arterial embolism arterial *thrombosis*	Acute anoxia of nerves	Excruciating pain in digits numbness sense *of* deadness	Stocking glove type of anesthesia or hypesthesia wrist or foot drop loss of voluntary *movement*	Invariably present to a marked degree
Diabetes heavy metal poisoning chronic alcoholism	Peripheral neuritis	*Discomfort* in legs & arms shooting burning pain coldness numbness tingling *prickling*	Impaired or absent vibratory sense hypesthesia anesthesia or hyperesthesia absent Achilles tendon or patellar reflex foot drop	None present
Cervical rib scalenus anticus hyperabduction and costoclavicular syndromes	Pressure on brachial plexus	Pain *paresthesia* numbness *in fingers*	Hypesthesia hyperesthesia slight weakness or even paralysis of muscles	Reduced or absent pulsations only when precipitating position *is assumed*
Causalgic states neuroma pressure *on* nerves in course of occupation	Pressure on or *injury* to peripheral nerves in limb	Severe *excruciating* lancinating burning pain	Signs of partial destruction of *nerves*	Signs of vasospasm present
Cervical osteoarthritis *cervical* or lumbar herniated disk sciatica	Pressure on peripheral nerves proximal to limb	Tingling *shooting* pain	Deep reflexes may be reduced or absent anesthesia or hypesthesia	None present

Nonvascular Disorders Manifesting Abnormal Neurologic Findings

In the differential diagnosis of vascular disorders associated with neuritic changes, it is also necessary to consider the various nonvascular conditions in which peripheral neuritis or pressure on peripheral nerves is part of the clinical picture Among these are diabetic neuritis, toxic (alcohol, lead or arsenic) neuritis vitamin deficiency neuritis, cervical arthritis, tumors within the spinal canal, protrusion of an intervertebral disk in the lumbar or cervical levels of the spinal column supraspinatus tendinitis, and subacute combined degeneration of the cord with or without pernicious anemia The absence of findings of an impaired arterial circulation, the existence of an etiologic factor, the effect of alteration of position or traction on initiating symptoms, and changes in the x ray should help in the separation of these entities from those having a vascular basis (See Table 7)

ENTITIES ASSOCIATED WITH PETECHIAE AND ECCHYMOSIS

Vascular Disorders

Since petechiae and ecchymosis may be noted in conjunction with peripheral vascular disorders, it is necessary to differentiate such findings from those observed in primary hematologic conditions or in other nonvascular diseases The underlying mechanism is either some change in the permeability of the capillaries allowing formed elements of the blood to enter the tissue spaces, an increase in vascular fragility or occlusion of minor vessels by very small emboli, followed by *damage to their walls and extravasation of* blood

The most common cause for petechiae in vascular disorders is a local state of anoxia which involves the capillary wall to produce a greater permeability of this membrane The resulting numerous fine discrete lesions or areas of ecchymosis are generally noted on the distal portion of the extremities The discoloration does not disappear *with the local application of pressure nor is it altered by elevation of* the extremity to permit drainage of blood out of the subpapillary venous plexus The permanence of the disturbance is related to the fact that it is due to an actual extravasation of blood However the range of color change generally associated with the breakdown of free hemoglobin in the skin and subcutaneous tissue is not noted in this type of change The findings may last for a relatively long period of time, or may, in fact, never vanish

Clinically *petechiae* and ecchymosis associated with local anoxia may be found in both arterial and venous disorders although much less often in the latter When such abnormalities are observed in arteriosclerosis obliterans they generally warrant an extremely guarded prognosis regarding the viability of the involved tissues Polyarteritis nodosa and disseminated lupus erythematosus may on occasion also manifest *individual or* confluent petechiae as a result of fine hemorrhages into the skin Similarly, in the severe degree of acute deep thrombophlebitis of the lower extremity, in which there is marked swelling areas of ecchymosis may be noted over the skin of the leg At times the lesions are so numerous and in such close proximity that they give the appearance of a large subcutaneous hemorrhage

Petechiae may appear in large crops in the distal portion of the lower extremities in individuals who become ambulatory after having been at complete bed rest for a relatively long time It is possible that a prolonged period of inactivity causes alterations in capillary permeability and that with the assumption of the upright position the resulting increase in hydrostatic pressure in the affected vessels is sufficient to produce a movement of blood through the capillary wall into the



FIG 6 (*Continued*) C Toxic purpura

tissue spaces Such changes are not related to any impairment in local arterial circulation and hence have little significance

Ecchymosis may on occasion be observed ...

... s with

... ince is

... these

... arterial occlusion pressure is applied locally this tendency is greatly magnified In fact extensive extravasation into the hands or feet may result In a sense the response following the use of a venous occlusion

Evidently stretching of the skin by the edema fluid is sufficient to prevent an adequate amount of nutrition from reaching it (For further discussion, see *Complications of the acute stage of deep thrombophlebitis* Chap XIV)

Nonvascular Status

In the differential diagnosis of petechiae and ecchymosis, it is necessary first to rule out the various thrombopenic (Fig 6A) and nonthrombopenic purpuras



Fig 6 Petechiae due to various nonvascular disorders A Positive Rumpel Leede test in a patient with thrombocytopenic purpura B Allergic purpura

Among the conditions in which the latter type is found are chronic nephritis cardiac or hepatic disease food allergy (Fig 6B) drug sensitivity vitamin C or P deficiencies metabolic disorders and infectious diseases (Fig 6C) particularly subacute bacterial endocarditis meningococcic meningitis measles typhoid fever and typhus fever Toxic doses of heparin and dicumarol may also be associated with fine petechiae particularly in the lower portion of the legs and in the feet Evidently in the presence of an exaggerated tendency to bleeding even minimal trauma is sufficient to elicit extravasation of blood



FIG 7 (*Continued*) F Fibrosarcoma G Nodule of Hodgkin s disease H Fibroma I Neurofibroma

Local trauma to the extremities is a common source of ecchymosis even in the absence of abnormalities of the blood or circulation This is particularly true in the case of the normal female with considerable deposition of subcutaneous adipose tissue The latter supplies very poor support to the capillaries traversing it and hence these vessels can be readily destroyed by minor injury

Rupture of large vessels in the extremities generally veins may occur spontane

the naked e To facilitate the count two circles about 5 mm in diameter are inscribed on the skin Normally each circle should contain 10 to o petechiae with increased capillary fragility the number may rise to as high as 100 or more (Fig 6A)

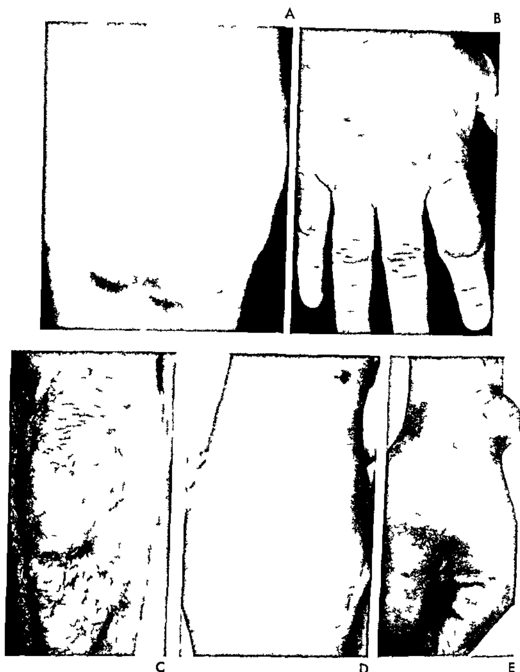


Fig 7 Examples of masses in the extremities A Cluster of varicose veins in the leg B Gouty nodule C Nodule of rheumatoid arthritis D Nodule of sarcoidosis E Ganglion

pressure can be considered as a positive Rumpel Leede test * while application of an arterial occlusion pressure evidently produces enough anoxia to cause further *increase in permeability of susceptible capillaries*

* This test which measures any increased tendency for petechial bleeding from capillaries is performed as follows [4] Using an ordinary blood pressure cuff capillary blood pressure is increased by obstructing venous return through the application of a pressure half way between the systolic and diastolic level This is maintained for 10 to 15 minutes and then released following which the number of petechiae appearing immediately below the level of the cuff is determined with

Pitting edema is soft is generally found first in the distal portion of a limb and is *readily* reduced by recumbency and elevation of the extremity Lymphedema is *much* more firm and is less affected by elevation If either condition persists unchecked for any period of time it may be converted into an irreversible process, fibroedema which has the appearance of elephantiasis (p 367) This type of change is not altered to any extent by elevation

EDEMA IN THE PRESENCE OF NORMAL ARTERIAL, VENOUS AND LYMPHATIC SYSTEMS

There are several physiologic factors which may produce swelling of the distal portion of an extremity among which are the prolonged maintenance of the limb in dependency without contractions of voluntary muscles and exposure to extremes of heat and cold For the most part the response is reversible after removal of the etiologic agent

Dependency and Immobility of the Limb

Edema resulting from maintaining the extremity in dependency for a long time is observed in a number of different conditions The paralyzed limb in the early stage of hemiplegia may demonstrate this type of change although it is possible that other factors such as disturbances in subcortical centers contribute to the state Another example is the swelling noted in the hands of the psychotic patient who insists on keeping his arms immobile against the sides of his body for hours or days Individuals who must continuously stand or sit in one position as in the course of their daily work or on automobile or train rides may develop edema in the lower extremities (traveller s edema deck ankles) This is first manifested by a sense of fullness in the foot and then actual discomfort as though the shoe has become too tight Examination will generally reveal definite swelling on the dorsum of the foot and around both malleoli and even on the lower portion of the leg The amount is usually not enough to permit pitting and it disappears after a night s rest with the extremities in the horizontal position (For a discussion of the underlying mechanism responsible for dependency edema see Physiologic Edema Chap XXVIII)

Exposure to Extremes of Environmental Temperature

In the summer months swelling of the ankles may occur normally a tendency which is exaggerated by prolonged standing or sitting particularly in stout or pregnant women Walking on a hot surface will have a similar effect (p 461)

Swelling of an extremity may also follow exposure to cold in individuals who [illegible] C [illegible] but [illegible] in the form of a drop in blood pressure a rise in pulse rate flushing of the face and an increase in gastric acidity The swelling of the exposed hand may be considerable and is invariably limited to the part previously immersed in the cold water It may persist for hours and even days afterward This alteration is usually associated with pain in the digits in the form of burning paresthesia and color changes in the whole hand Because of the close resemblance

ously or following trauma A common site for this type of abnormality is deep in the calf muscles Usually changes in skin color are noticed several days after the acute episode as a result of the appearance of the breakdown products of hemoglobin in the cutaneous lymphatic channels In most instances the level of such alteration is some distance below the actual point at which the hemorrhage took place Very rarely are the constituents of blood themselves observed in the skin

CUTANEOUS AND SUBCUTANEOUS MASSES

A number of different clinical entities are associated with or characterized by palpable masses in the extremities In some the nodules are merely one facet of a generalized condition while in others they are the sole indication of the existence of the disorder On the basis of pathogenesis and structures involved, the entities in which such abnormalities occur can be divided into several categories One group has in common a varying degree of acute or chronic panniculitis in the subcutaneous tissues, as typified by the panniculitis of Weber Christian disease, erythema induratum erythema nodosum, erythrocyanosis, and chronic pernio (Fig 50 p 332) Another consists of entities in which the main involvement is in the venous system, as for example thrombophlebitis migrans (Fig 31 p 238) benign superficial thrombophlebitis (Fig 30 p 235) a cluster of varicose veins (Fig 7A), and chronic indurated cellulitis following prolonged venous stasis Masses resulting from changes in the arterial side of the circulation are characterized by the glomus tumor hemangioma polyarteritis nodosa arterial aneurysm (Fig 39 p 292) and congenital and acquired arteriovenous fistulas (Fig 58 p 370) Finally there are such nonvascular conditions as fatty tumors neurofibromas and sarcoidosis which also among others are associated with nodular lesions in the extremities (Fig 7D, I) The pertinent data with regard to the differential diagnosis of these various disorders are summarized in Table 8

As a number of the above conditions have certain features in common at times it is difficult or even impossible to distinguish them from each other on purely clinical grounds Hence it may be necessary to resort to histopathologic study of biopsy material although even this procedure does not always establish the true basis for the lesion

SWELLING

Swelling of the extremities can result from a number of different factors some physiologic some peripheral vascular and others unrelated to any local pathology in the limbs (Table 9) Regardless of the cause the patient suffering from any degree of edema generally complains of heaviness and a sense of tiredness in the involved extremity due to the increased weight from the accumulation of fluid in the tissues (For physiologic basis or pathogenesis see *Edema* Chap XXVIII)

Swelling can be grossly divided into two types easily pitting edema and non pitting edema (lymphedema) At times both may be present in the same limb

Pitting edema is soft is generally found first in the distal portion of a limb and is readily reduced by recumbency and elevation of the extremity Lymphedema is much more firm and is less affected by elevation If either condition persists unchecked for any period of time it may be converted into an irreversible process fibroedema which has the appearance of elephantiasis (p 567) This type of change is not altered to any extent by elevation

EDEMA IN THE PRESENCE OF NORMAL ARTERIAL VENOUS AND LYMPHATIC SYSTEMS

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Exposure to Extremes of Environmental Temperature

In the summer months swelling of the ankles may occur normally a tendency which is exaggerated by prolonged standing or sitting particularly in stout or pregnant women Walking on a hot surface will have a similar effect (p 461)

Swelling of an extremity may also follow exposure to cold in individuals who are sensitive to this agent Generally immersion of the hands in water at 8°–10° C (46.4°–50 F) for 5 minutes is enough to produce not only the local change but also systemic reactions in the form of a drop in blood pressure a rise in pulse rate flushing of the face and an increase in gastric acidity The swelling of the exposed hand may be considerable and is invariably limited to the part previously immersed in the cold water It may persist for hours and even days afterward This alteration is usually associated with pain in the digits in the form of burning paresthesia and color changes in the whole hand Because of the close resemblance

Table 8 Differential Diagnosis of Cutaneous

Clinical entities in which change is found	*Characteristics of lesion*	*Appearance of overlying skin*	*Necrosis ulceration or suppuration*	*Usual location of lesion*	*Other less frequent sites of lesions*
Thrombophlebitis migrans	Single or multiple cordlike nodules in superficial veins about 2-5 cm long & 1 cm wide	Local signs of inflammation-redness and increased cutaneous *temperature*	None	Legs feet	Forearms hands *abdom*inal wall
Superficial benign *thrombo*phlebitis	Cord-like lesions involving relatively *long* portions of superficial veins generally single	Signs of inflammation-*redness and* increased cutaneous temperature	None	A single leg with possible extension into thigh	Feet
Chronic indurated cellulitis secondary to persistent *venous* stasis	Plaque-like areas of induration of *skin & subcuta*neous tissue of various sizes-single or mul*tiple thrombosed* superficial veins may be felt	Brawny change signs of chronic inflammation	Area may break down to form an ulcer	Lower third of legs proximal to medial malleolus	Remainder of leg
Acute cellulitis	Area of acute induration involving skin & subcutaneous tissue	Definite signs of acute inflammation-redness local swelling heat	Generally none	Lower third of leg and dorsum of foot	
Polyarteritis nodosa	Subcutaneous nodule at times pulsating	Normal	None	Along course of main arteries and their branches	
Arterial and arteriovenous aneurysms	*Pulsating masses* of various sizes with a bruit and a thrill	*In a. v* aneurysm skin may be warmer than *normal* & pink in color	*None unless* lesion enlarges rapidly and causes pressure necrosis	*In any* site where large vessels are situated	

and Subcutaneous Masses in Extremities

Gross involvement of local arterial venous or lymphatic system	*Systemic responses or changes*	*Pain*	*Histopathologic changes or pathogenesis*	*Sex or race differences*
No involvement of arteries signs of thrombosis of superficial veins	Generally none or of a mild degree	Spontaneous pain absent tenderness present over lesion or on movement or stretching of tissues	Occlusion of lumen of vein by cellular thrombosis with extensive infiltration of wall absence of inflammatory reaction of tissue in neighborhood of vein absence of necrosis of fat & of fibrosis	Occurs predominantly in males
No involvement other than of superficial veins	Generally none	Generally none unless involved portion is moved or stretched	Thrombosis of vein with phlebitis and periphlebitis destruction of valves	None
Generally venous involvement—varicosities or old ilio femoral thrombophlebitis	Generally none	Tenderness on movement of involved part	Vasculitis and fibrosis with panniculitis	None
Lymphangitis lymphadenitis	Generally a rise in temperature malaise	May be severe at rest exaggerated with movement	Inflammatory changes in tissues	None
Generally not present	Almost always present — fever changes in kidneys hypertension g i & neurologic involvement	Not present over lesions may be present in muscles	Involvement of all coats of artery with necrosis of wall leading to aneurysmal formation	Common in males in fourth or fifth decade
Reduction in pulsations below a v aneurysm increase in size of veins proximally	Patient may develop congestive failure if a v aneurysm is large & is close to heart	None unless pressure is applied	In case of a v aneurysm—communication between artery and vein following trauma histologic signs of destruction of continuity of vessels	None

Table 8

Clinical entities in which change is found	*Characteristics of lesion*	*Appearance of overlying skin*	*Necrosis ulceration or suppuration*	*Usual location of lesion*	*Other less frequent sites of lesions*
Glomus tumor	Small round subcutaneous nodules 3-5 mm in diameter	May be cyanotic or red	None	Tips of fingers and toes (subungual)	Forearm arm & leg
Panniculitis (Weber-Christian disease)	Single or multiple crops of large subcutaneous plaques & nodules 0 5-3 0 mm in diameter	First red or violaceous depression of skin due to subcutaneous atrophy	Nodules may become necrotic but do not suppurate	Thighs legs abdomen breasts and arms	Rest of body
Chronic pernio	Hard painful nodules appearing with onset of cold weather & generally disappearing in summer	Redness thinning out of skin violaceous color	Ulceration almost invariably present	Legs lower third	Rest of leg and hands
Erythema induratum (Bazin s disease)	Nodules 5-15 cm in diameter	Red or violaceous turning brown	Ulceration frequently present irregularly shaped ragged undermined edge	Calves of legs	Arms
Erythema nodosum	Relatively superficial firm tender lesions 1-2 cm in diameter	Erythema edema & then bruised appearance ecchymosis may be present	Lesions may fluctuate but do not suppurate	Legs and forearms	Soles of feet calves thighs upper part of arms
Sarcoidosis	Small firm cutaneous nodules smooth & sharply demarcated	Brown or blue with small yellow granules at margin	Lesions do not suppurate or become necrotic	Face arms hands back	
Varicosities	Soft reducible mass which collapses on elevation	Blue	Occasional rupture & bleeding	Lower extremities	Occasionally on upper extremities

(continued)

Gross involvement of local arterial venous or lymphatic system	*Systemic responses or changes*	*Pain*	*Histopathologic changes or pathogenesis*	*Sex or race differences*
None	None	Excruciating pain on exposure to heat or cold or with pressure	Dilated vascular channels rich innervation of sympathetic nerves exaggeration of normal glomus	None
None	Recurrent episodes of fever as high as 40°0 C (104°F)	Nodules may be tender or painless	Edema & necrosis of subcutaneous fat with inflammatory cellular infiltra tion (panniculitis) of subcutaneous tissue	Chiefly in obese females between second & fourth decades
None	Fever present occasionally	Excruciating pain while lesion is forming less pain later	Angiitis of smaller vessels giant cells & panniculitis no signs of tuberculosis	Chiefly in females
None of large vessels	Findings of tuberculosis elsewhere in majority of patients	Lesion is painful	Typical tubercles may be present or a severe degree of panniculitis or fibrosis rather than necrosis of fat varying degrees of panarteritis & phlebitis may be present	Chiefly in young females
None	Fever malaise & migratory arthritis of various joints of extremities	No pain but nodules are tender	Infiltration of lymphocytes and polymorphonuclear leukocytes about the vascular network in skin panniculitis also present	Chiefly in *females*
None	Slight con stitutional symptoms lymphade nopathy	None	Collections of epi thelioid cells in the form of nodules not sharply defined from normal tissue	Predilec tion for Negroes
Signs of incompetency of venous valves	None	None	Incompetent valves with regurgitant flow	Present more often in females

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Clinical entities in which change is found	*Characteristics of lesion*	*Appearance of overlying skin*	*Necrosis ulceration or suppuration*	*Usual location of lesion*	*Other less frequent sites of lesions*
Glomus tumor	*Small round* subcutaneous nodules 3-5 mm in diameter	*May* be cyanotic or red	*None*	Tips of fingers and toes (subungual)	Forearm arm & leg
Panniculitis (Weber-Christian disease)	Single or multiple crops of large subcutaneous plaques & nodules 0 5-3 0 mm in diameter	First red or violaceous depression of skin due to subcutaneous atrophy	Nodules may become necrotic but do not suppurate	Thighs legs abdomen breasts and arms	Rest of body
Chronic pernio	Hard painful nodules appearing with onset of cold weather & generally disappearing in summer	Redness thinning out of skin violaceous color	Ulceration almost invariably present	Legs lower third	Rest of leg and hands
Erythema induratum (Bazin s disease)	Nodules 5-15 cm in diameter	Red or violaceous turning brown	Ulceration frequently present irregularly shaped ragged undermined edge	Calves of legs	Arms
Erythema nodosum	Relatively superficial firm tender lesions 1-2 cm in diameter	Erythema edema & then bruised appearance ecchymosis may be present	Lesions may fluctuate but do not suppurate	Legs and forearms	Soles of feet calves thighs upper part of arms
Sarcoidosis	Small firm cutaneous nodules smooth & sharply demarcated	Brown or blue with small yellow granules at margin	Lesions do not suppurate or become necrotic	Face arms hands back	
Varicosities	Soft reducible mass which collapses on elevation	Blue	Occasional rupture & bleeding	Lower extremities	Occasionally on upper extremities

SWELLING

(continued)

Gross involvement of local arterial venous or lymphatic system	*Systemic responses or changes*	*Pain*	*Histopathologic changes or pathogenesis*	*Sex or race differences*
None	None	Generally symptomless occasional aching or cramping of muscles	A constitutional abnormality of aponeurosis—either a defect of fibrous layer or impaired ability to withstand distension trauma may produce it	Generally in young athletic males
None	None	None	Fatty tumors	None
None	Changes associated with syphilis	None	Histologic findings of a gumma	None

After the edema of the acute stage has subsided there may be a recurrence of swelling when ambulation is resumed (Fig 36 p 277) At first it is pitting in type increasing during the course of a day s physical activity and being particularly affected by the amount of time the patient spends in the upright position In the morning it is generally much less and may even be absent In those instances in which an effective collateral venous circulation develops there is a gradual reduction in edema However if this does not take place and no attempts are made to control the swelling a nonpitting lymphedema will form which is not affected materially by elevation of the limb Associated with this type of change are brawniness induration and brown pigmentation of the skin

If the patient is first seen when lymphedematous changes have already occurred the differential diagnosis may be difficult particularly if the acute episode had taken place years before and the details are no longer recalled very clearly by the patient Signs of occlusion of a main venous channel may not be obvious at this stage and it may be necessary therefore to resort to venography to determine whether or not a block is present Performance of a venous pressure measurement (p 406) in one of the superficial veins of the foot is also of value since a greater than normal reading in the upright position and with exercise indicates that interference in venous outflow exists in the limb and hence that the lymphedema is related to this factor rather than to involvement of lymphatics on some other basis

Swelling of the hand and forearm is a constant and early sign of sudden thrombosis of the axillary vein (p ~39) It is associated with the onset of pain and the

Table 8

Clinical entities in which change is found	Characteristics of lesion	Appearance of overlying skin	Necrosis ulceration or suppuration	Usual location of lesion	Other less frequent sites of lesion
Fascial hernia of muscles	Small circumscribed often bilaterally symmetrical nodules nontender soft & easily reducible	Normal	None	About 15 cm above malleoli—middle third of leg lateral side of anterior border of tibia	
Nodular circumscribed lipomatosis	Nodular encapsulated lipomas single or multiple soft	Normal	None	No specific sites	
Syphilis	Subcutaneous circumscribed nodule—becomes attached to skin	Reddish brown	Lesion tends to ulcerate	Upper half of leg	Thigh face and neck

of the local and systemic responses in cold allergy to those produced by the parenteral administration of histamine it has been suggested that the liberation of this agent in the tissues is responsible for the clinical picture[1]

PERIPHERAL VASCULAR DISORDERS PRODUCING EDEMA

Interference with Venous Outflow

Among the conditions which interfere with the movement of blood out of an extremity and hence initiate or contribute to local swelling are disorders affecting the veins themselves and states in which extrinsic pressure is exerted on these vessels

Local Involvement of the Venous System In the initial stage of acute deep thrombophlebitis of the lower extremities a pitting type of edema is a prominent finding (Fig 32 p 246) However in severe cases the skin is so tightly stretched by the fluid in the tissue spaces that pitting is accomplished only with difficulty The history of an acute onset of swelling associated with the presence of pain in the groin and along the course of the femoral vein, signs of vasospasm distended superficial veins, and systemic reactions should help differentiate this type of response from edema due to other causes Generally the change is noted in one extremity although if the occlusion had occurred originally at the bifurcation of the inferior vena cava or if propagation had taken place to that level both sides may be involved (For discussion of factors involved in production of edema see *Pathologic Edema* Chap XXVIII)

(continued)

Cross involvement of local arterial venous or lymphatic system	Systemic responses or changes	Pain	Histopathologic changes or pathogenesis	Sex or race differences
None	None	Generally symptomless occasional aching or cramping of muscles	A constitutional abnormality of aponeurosis—either a defect of fibrous layer or impaired ability to withstand distension trauma may produce it	Generally in young athletic males
None	None	None	Fatty tumors	None
None	Changes associated with syphilis	None	Histologic findings of a gumma	None

After the edema of the acute stage has subsided there may be a *recurrence* of swelling when ambulation is resumed (Fig 36 p 277) At first it is pitting in type increasing during the course of a day's physical activity and being particularly affected by the amount of time the patient spends in the upright position In the morning it is generally much less and may even be absent In those instances in which an effective collateral venous circulation develops there is a gradual reduction in edema However if this does not take place and no attempts are made to control the swelling a nonpitting lymphedema will form which is not affected materially by elevation of the limb Associated with this type of change are brawniness induration and brown pigmentation of the skin

If the patient is first seen when lymphedematous changes have already occurred the differential diagnosis may be *difficult* particularly if the acute episode had taken place years before and the details are no longer recalled very clearly by the patient Signs of occlusion of a main venous channel may not be obvious at this stage and it may be necessary therefore to resort to venography to determine whether or not a block is present Performance of a venous pressure measurement (p 426) in one of the superficial veins of the foot is also of value since a greater than normal reading in the upright position and with exercise indicates th[illegible] ference [illegible]

[illegible] is a constant and early sign of sudden thrombosis of the axillary vein (p [illegible]79) It is associated with the onset of pain and the

appearance of vasospasm Little difficulty should be encountered in determining the cause of the edema Of prime importance in this regard is the visualization of the rapidly forming collateral venous network extending onto the chest wall For this purpose infrared photography or venography is of great advantage The history of a repeated movement which places a strain on the arm and shoulder should also help make the diagnosis

The swelling associated with varicosities of the lower extremities is generally of a minor degree, being limited to sites around the ankles or lower portion of the leg It does not readily pit, is related to the length of time the patient is on his feet and is usually minimal after a night's rest The finding is often associated with other signs of venous stasis, such as pigmentation and induration of the skin Determination of the existence of varicose veins should present no difficulty if the extremity is carefully examined in different positions and if the various tests for competency of the valves in the superficial veins are performed

Extrinsic Pressure on Main Venous Channels In the lower extremity, pressure on the iliofemoral or common iliac veins may produce local edema Therefore in the presence of swelling of one or both limbs for which there is no apparent etiology, the pelvis should be carefully examined for the presence of masses In the female, a vaginal examination should be done to rule out the existence of tumors pregnancy, or fibrous bands In the male a rectal examination may help determine the cause for the edema At times, it may be necessary to give the patient a barium enema on the possibility that a tumor might be producing distortion of the outline of the large bowel which could be identified by the x ray An intravenous pyelogram may also be of value

In the case of swelling of the hand and forearm not due to local mechanisms, one must seek the etiologic factor in the mediastinum as for example partial or complete occlusion of the superior vena cava or its main tributaries by pressure from tumors in this location Under such circumstances the findings in the upper extremities are associated with signs of increased venous pressure in the neck and face X rays taken in various positions and venography may both be helpful in determining the basis for interference with venous return to the heart Venography will not only outline the superior vena cava, and thus visualize any extrinsic distortion of its lumen but it may also help make apparent any intrinsic pathology

Interference with Lymphatic Drainage

One of the most common causes of swelling of the extremities is interference with the movement of lymph out of the limb This may occur as the result of obstruction or destruction of lymphatic channels of the nodes into which they drain or of both In the well-established case the edema is of the nonpitting type which is reduced only slightly by prolonged elevation of the extremity

Among the various etiologic factors responsible for lymphedema are inflammatory disorders (erysipelas and cellulitis) radical mastectomy, elephantiasis and primary obstruction of the larger vessels by congenital abnormalities (Fig 55 p 360) Metastasis to the local lymph nodes and the lymph channels will also result in interference with lymphatic drainage and the formation of swelling (Fig 56 p 361) In each instance the history of the onset of the lymphedema, its relationship

to injury and the presence or absence of associated inflammation or malignancy are points of value in the differential diagnosis of such a finding (For further discussion of lymphedema see Chap XXII)

INTERFERENCE WITH ARTERIAL INFLOW

Severe Structural Changes Although ordinarily a patient with arteriosclerosis obliterans or thromboangiitis obliterans does not manifest edema of the lower extremities he may if he is suffering from impending or existing gangrene and has learned that dependency of the involved limb will bring about relief from pain Little difficulty should be encountered in determining the cause of this type of swelling for signs of markedly reduced arterial circulation are always present together with the findings of nutritional disturbances (Fig 8) (For basis for swelling see p 462 for treatment see p 403)



Fig 8 Edema associated with ulceration and gangrene due to arteriosclerosis obliterans and diabetes

Arterial Vasospasm Under certain circumstances edema of the distal portions of an extremity is produced by arterial vasospasm This may be present to a marked degree in the acute phase of frostbite (Fig 47 p 326) and as a chronic manifestation of posttraumatic vasomotor disorders (Figs 4 and 43 pp 312 and 313) and causalgic states It is a question as to whether the swelling in the last two conditions is due entirely to vasospasm or whether the associated disuse and immobility of a limb in a dependent position do not also contribute to this state In this regard it is of interest that active and passive movements and elevation as well as removal of vasomotor tonus may cause a disappearance of the edema in these disorders (For pathogenesis see *Pathologic Edema* Chap XXVIII)

SYSTEMIC NONVASCULAR CONDITIONS PRODUCING EDEMA

There are a number of systemic disorders which manifest as one facet of their clinical picture swelling of the extremities most often of the lower ones Among these are congestive heart failure cirrhosis of the liver nephrosis hypothyroidism and nutritional disorders In none of these entities are local signs of lymphatic venous or arterial involvement found However the peripheral pulses may not be readily palpable because of the presence of the edema

Congestive Heart Failure Edema associated with congestive heart failure is invariably present in both lower extremities although not necessarily to the same degree If a limb has an underlying impaired arterial or venous circulation the

Table 9 Differential Diagnosis of Swelling in Extremities

States or clinical entities in which change is found	*Underlying mechanism or pathogenesis*	*Initiating factor*	*Differential points in history*	*Differential points in physical findings*	*Diagnostic procedures*
Prolonged standing or sitting in normal people (traveller s edema deck ankles) compulsion hysteria early stage of hemiplegia application of cast	Increased capillary pressure due to effect of hydrostatic pressure decreased venous outflow	Dependency and immobility of extremity	History of maintaining extremity in dependency for long periods of time	Pitting edema of distal portion of limb no signs of arterial venous or lymphatic impairment	
Heat edema	Increased capillary filtration pressure due to dilatation of arterioles	Exposure to heat	History of exposure to high environmental temperature particularly in case of obese females	Pitting edema of feet no signs of venous arterial or lymphatic involvement	
Cold allergy	Increased capillary permeability due to anoxia of wall following vasoconstriction of arterioles formation of histamine locally	Exposure to cold	History of exposure of involved portion to cold for a relatively short period of time	Pitting edema of part of limb exposed no local signs of venous arterial or lymphatic involvement drop in blood pressure rise in pulse rate	Increase in gastric juice
Acute deep thrombophlebitis of lower extremity axillary vein thrombosis	(1) Increased capillary filtration pressure due to markedly elevated local venous pressure (2) reduced lymphatic outflow due to obstruction of main lymphatic channels (3) reduced lymphatic outflow due to loss of purping action supplied by distension & recoil of large arteries	Acute thrombosis of main venous channel	History of sudden onset of marked swelling of distal 2/3 or entire limb associated with severe pain along course of involved vein	In lower extremity marked pitting edema tenderness in groin & inner side of thigh prominent superficial veins signs of vasospasm fever tachycardia increased sed rate and wbc In upper extremity tenderness in axilla and along course of axillary vein, and pitting edema	Venogram may demonstrate block in venous system increased venous pressure in foot or hand

Table 9 (continued)

States r clinical entities n which change is found	*Underlying mechanism or pathogenesis*	*Insti ting factor*	*Differential points in history*	*Differential points in physical findings*	*Diagnostic Procedures*
Postphlebitic *syndrome* occa sionally sequel *of* axillary vein *thrombosis*	Increased capillary filtration pressure *due to* elevated local venous pressure	Incompetency or *chronic obstruction* of main venous channels	*History of* deep thrombophlebitis in past *history* of re duction in swelling *with* bed rest & ele vation & *increase* with dependency	Pitting edema pigmen tation varicos*ities* vasospasm possibly trophic changes	Venogram may *demonstrate* old blocked portion & bridging collater-*als infrared pho* tography will bring out superficial venous collater-*als increased* venous pressure in foot
Varicosities	*Increased* capillary filtration pressure due to venous stasis	Incompetency of valves in super-ficial veins	History *of* feeling *of* heaviness and tiredness on standing	Slight pitting or non-pitting edema around ankles pigmen*tation* induration of skin even *trophic changes*	*Various tests show* incompetency of valves in super ficial veins
Masses in medias *tinum or* in pelvis ascites	Increased capi*llary* filtration pressure following *increase* in *local venous pressure*	Pressure on main venous channels	History of painless *swelling* of one or both extremities	Pitting edema *of distal* portion of extremity *no signs of arterial* or lymphatic impair-*ment no* varicosities	*Increased* venous pressure venogram may outline site of compression *x-ray* ivp & barium *enema* may demonstrate mass in pelvis
Injury to consid erable portion of circumference *of limb surgical* procedures re quiring excision *of regional lymph* nodes roentgen & *radium* therapy	*Impairment* in removal of *lymph* because of a reduction in the number of functioning lymph channels or *rodes*	Trauma to lymph channels *or rodes*	History of injury to *extremity involving* skin and subcuta neous tissue fol-lowed by appearance of painless edema	*Nonpitting or slightly* pitting edema below *level* of trauma *no* arterial or venous *impairment*	Trabeculations in soft tissue using soft tissue x-ray technique *venous* pressure & veno *gram normal*

Table 9 (continued)

States or clinical entities in which change is found	*Underlying mechanism or pathogenesis*	*Initiating factor*	*Differential points in history*	*Differential points in physical findings*	*Diagnostic procedures*
Repeated attacks of cellulitis or erysipelas with lymphangitis filariasis infectious diseases	Lymph stasis because of thrombosis of lymph channels	Inflammatory processes	History of dermatophytosis with repeated attacks of cellulitis of foot lymphangitis and lymphadenitis	Nonpitting edema of foot signs of chronic infection may be present	Venogram and venous pressure normal trabeculation in soft tissues as seen in x-ray
Lymphosarcoma carcinoma	Impairment of removal of lymph because of block in lymph nodes	Metastasis to lymph nodes	History of appearance of painless swelling beginning in thigh and progressing distally	Enlarged hard regional lymph nodes nonpitting edema & brawny induration signs of original lesion	Venogram & venous pressure normal biopsy of gland helpful in making diagnosis
Lymphedema praecox congenital lymphedema (simple and hereditary)	Impairment of removal of lymph because of obstruction or underdevelopment of lymph channels	No apparent factor	History of appearance of painless progressive swelling shortly after birth or after puberty familial history in some instances absence of history of local infections	Pitting or nonpitting edema indurated and brawny skin no signs of venous or arterial impairment	Venogram and venous pressure normal
Severe degree of arteriosclerosis obliterans and thromboangiitis obliterans with gangrene or ulceration	(1) increased capillary filtration pressure due to additive effect of hydrostatic pressure (2) increased capillary permeability due to anoxia of wall following impaired arterial circulation	Prolonged maintenance of limb in dependency	History of severe pain associated with trophic change and relief on placing limb in dependency	Pitting edema of foot marked signs of arterial impairment trophic change present	Venogram and venous pressure normal arteriogram shows block in main arterial channel
Frostbite posttraumatic vasomotor disorder causalgia possibly sequel of anterior poliomyelitis	Increased capillary permeability due to anoxia of wall following vaso constriction of arterioles	Vasospasm	History of onset of original lesion	Pitting edema of distal portion of limb signs of original lesion & presence of increased sympathetic tone — hyperhidrosis coldness cyanosis	Venogram and venous pressure normal

Table 9 (continued)

States or clinical entities in which change is found	*Underlying mechanism or pathogenesis*	*Initiating factor*	*Differential points in history*	*Differential points in physical findings*	*Diagnostic procedures*
Nephrosis nephri tis cirrhosis of liver nutrition al disturbances	Increased movement of fluid out of capillaries due to reduced osmotic resistance of blood proteins	Deficient proteinemia	History of onset of original condition	Pitting edema both lower extremities signs of original condition	Low total protein in blood — loss of albumin in urine liver profile may show impairment of liver function
Congestive heart failure	(1) increase in capillary filtration pressure due to increased central ven ous pressure (2) reten sion of salt & fluids in tissue spaces (3) in creased circulating blood volume	Impaired cardiac function	History of onset of original condition	Pitting edema both lower extremities signs of congestive heart failure no signs of local venous impairment	High central venous pressure
Lipodystrophy	Possibly some venous stasis	Deposition of fat and fluid	History of deposition of fat in lower ex tremities & buttocks & not elsewhere some reduction in swelling after night s rest	Nonpitting edema both lower extremities no signs of venous arterial or lymphatic involvment	Venogram and venous pressure normal
Myxedema	Deposition of myxedem atous material in subcutaneous tissue	Lowered basal metabolism	History of painless swelling slowly changing texture of skin and other symp toms of reduced metabolism	Nonpitting swelling of both lower extrem ities changes in consistency of skin other signs of lowered metabolism	High blood cholesterol low basal metabolism
Cong nital arteriovercus fistula	Enlargement of bones and of muscles (in part due to hypertrophy and in part to dilated arterial channels)	Communi- cations between arterial and venous channels	History of enlarge ment of limb from time of birth slowly growing painless	Nonpitting enlargement of digits or a limb other signs of con genital a v fistula	High pressure in veins locally and high content of oxygen in local venous blood

amount of swelling in it may be greater than in the otherwise normal one Furthermore, its response to therapeutic means for removal of the fluid may be much slower, which may on occasion temporarily result in the presence of unilateral edema The swelling of congestive heart failure pits except when it is so massive that the skin is stretched taut by it Bed rest and elevation of the limb may reduce this type of edema somewhat, but not to the extent noticed with that of primary venous origin Of course, if the function of the heart is improved by such a regimen the swelling will become much less on this account rather than because of the position of the extremity At the same time, standing does not have as much an effect on increasing the edema as it does in the case of the limb with a reduced venous efficiency The presence elsewhere of the cardinal signs of cardiac weakness the involvement of both lower extremities, and the absence of findings of venous obstruction locally help differentiate the pitting edema of congestive heart failure from swelling due to other causes (For pathogenesis see *Congestive Heart Failure* Chap XXVIII)

Cirrhosis of the Liver The edema associated with cirrhosis of the liver is pitting in type and may be considerable It is generally accompanied by other signs of this disorder, namely, a history of alcoholism and dietary indiscretions and the presence of ascites an enlarged liver and spleen vascular spiders and extensive collateral venous channels on the abdominal wall A reversal of the A/G ratio with a reduction of the total protein level in the blood, and other abnormalities of liver function help support this diagnosis

Nephrosis Edema of the lower extremities due to nephrosis is similar in all regards to that present with cirrhosis or heart failure The differentiation therefore rests on other findings such as the history of a renal disorder a high blood cholesterol, a low blood total protein and a reversal of the A/G ratio associated with the loss of large quantities of albumin in the urine and other abnormal urinary and blood constituents

Hypothyroidism Patients manifesting a low metabolic rate and other stigmata of hypothyroidism may also demonstrate swelling of the feet and lower portions of the legs This response is not related to the period of time they are on their feet but instead may be found in the morning on arising The edema is generally of the nonpitting type Whether or not it is an indication of the deposition of myxedematous material in the subcutaneous tissue and the skin is difficult to state

Nutritional Edema (War Edema) Differences of opinion exist with regard to the mechanisms responsible for the swelling of the extremities associated with an inadequate diet Whether protein deficiency vitamin deficiency or both are etiologic agents can not be stated with certainty While it has been generally considered that a total blood protein of 5–5 5 Gm per 100 cc and an albumin concentration of 2 5–3 0 Gm per 100 cc are critical levels below which edema can be expected recently the role of hypoproteinemia in the pathogenesis of war edema has been challenged[3] In any event in most instances low total protein values are found The swelling is generally of a pitting type and may be associated with ascites and hydrothorax

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CHAPTER

VII DIFFERENTIAL DIAGNOSIS OF PHYSICAL FINDINGS (*Continued*)

2. ULCERATION, GANGRENE

ULCERATION

The most frequent causes for ulceration in an extremity are a marked impairment in cutaneous arterial blood flow and interference with venous outflow. However, it must be borne in mind that there are a number of nonvascular conditions in which this type of lesion may also be found. Both categories are discussed below.

Ulceration of Arterial Origin

Organic Arterial Vascular Disorders

Basis for Lesion. When a reduction in arterial inflow reaches a level at which the nutrition brought to the tissues of the extremities is inadequate for resting metabolic needs, then minimal trauma or a slight infection may be enough to initiate an ulcer (Table 10). Such a state of anoxia is usually the result of structural abnormalities in the wall of the main arteries, producing a marked decrease in cutaneous blood flow. Since the latter change is ordinarily most prominent in the distal portions of the limb, it is understandable why the heel or the digits of the hand and foot are frequent locations for an ischemic ulcer. However, the lesion may also be present elsewhere, as for example on the leg and forearm, provided these portions are subjected to trauma of sufficient magnitude to cause destruction of tissue. In such locations the process may penetrate deep fascia to expose muscles and tendons (Fig. 9A).

Clinical Characteristics. The ischemic ulcer usually produces severe pain locally. This may be due in part to irritation or destruction of small sensory fibers by the surrounding inflammatory reaction, and in part, to the underlying marked anoxia of tissue. Signs of a definitely impaired local arterial circulation are invariably present. A systemic response is generally not elicited except in the patient who is also suffering from diabetes mellitus. Under the latter circumstances, secondary infection of the ulcer is common and this may lead to lymphangitis, lymphadenitis, and fever.

Because a marked reduction in cutaneous blood flow is usually associated with a concomitant change in muscle circulation, a patient with an ischemic ulcer will in most instances also complain of intermittent claudication in the leg or foot. In the absence of this symptom, the sudden appearance of a nutritional disturbance



FIG 9 Ulcers of vascular and nonvascular origin A Thromboangiitis obliterans B Sickle cell anemia C Syphilis D Distension of skin by edema fluid of congestive heart failure E F itious lesion

should be viewed with the gravest concern since it most likely indicates th presence of a rapidly progressing occlusive process However this does not app to the diabetic with arteriosclerosis obliterans in whom the major involveme may be in the smaller arteries of the foot particularly to skin with only min circulatory impairment to the calf muscles (See *Role of diabetes mellitus* arteriosclerosis obliterans Chap IX)

CHAPTER

VII DIFFERENTIAL DIAGNOSIS OF PHYSICAL FINDINGS (*Continued*)

2. ULCERATION, GANGRENE

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FIG 9 Ulcers of vascular and nonvascular origin A Thromboangiitis obliterans B Sickle cell anemia C Syphilis D Distension of skin by edema fluid of congestive heart failure E Factitious lesion

should be viewed with the gravest concern since it most likely indicates the presence of a rapidly progressing occlusive process *However this* does not apply to the diabetic with arteriosclerosis obliterans in whom the major involvement may be in the smaller arteries of the *foot particularly to* skin with only minor circulatory impairment to the calf muscles (See *Role of diabetes mellitus* in arteriosclerosis obliterans Chap IX)

CHAPTER

VII DIFFERENTIAL DIAGNOSIS OF PHYSICAL FINDINGS (*Continued*)

2. ULCERATION, GANGRENE

ULCERATION

The most frequent causes for ulceration in an extremity are a marked impairment in cutaneous arterial blood flow and interference with venous outflow. However, it must be borne in mind that there are a number of nonvascular conditions in which this type of lesion may also be found. Both categories are discussed below.

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Basis for Lesion. When a reduction in arterial inflow reaches a level at which the nutrition brought to the tissues of the extremities is inadequate for resting metabolic needs, then minimal trauma or a slight infection may be enough to initiate an ulcer (Table 10). Such a state of anoxia is usually the result of structural abnormalities in the wall of the main arteries producing a marked decrease in cutaneous blood flow. Since the latter change is ordinarily most prominent in the distal portions of the limb, it is understandable why the heel or the digits of the hand and foot are frequent locations for an ischemic ulcer. However, the lesion may also be present elsewhere, as for example on the leg and forearm, provided these portions are subjected to trauma of sufficient magnitude to cause destruction of tissue. In such locations the process may penetrate deep fascia to expose muscles and tendons (Fig. 9A).

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Because a marked reduction in cutaneous blood flow is usually associated with a concomitant change in muscle circulation, a patient with an ischemic ulcer will, in most instances, also complain of intermittent claudication in the leg or foot. In the absence of this symptom, the sudden appearance of a nutritional disturbance

invariably the process penetrates the deep fascia The result is an irregularly shaped painful trophic disturbance varying in size from a pinhead to a lesion covering a considerable portion of the leg (Fig 38A p 282) The base is usually covered by a dirty exudate from which different types of organisms may be cultured A concomitant foul odor is a common finding The surrounding area is generally scaly indurated swollen markedly pigmented and has a purplish hue when the limb is in dependency There may be a secondary infection which is manifested by signs of inflammation around the ulcer

Varicose Ulcer The ulceration due to primary varicosities may resemble that which follows deep thrombophlebitis and at times it is difficult to differentiate between the two However the former is usually more superficial rarely penetrating the deep fascia and less resistant to therapy (Fig 38B and C pp 282 and 283) Furthermore no history can be elicited of an acute episode of marked swelling of the limb associated with systemic responses as is present in the case of deep thrombophlebitis At times it may be necessary to resort to venography and venous pressure measurements with exercise (p 476) to determine whether or not a block exists in the deep venous system The demonstration of a regurgitant flow in the superficial vessels is of no value as a differential point since this situation may be present both in varicosities secondary to incompetency of the deep venous system and in the primary type (For the treatment of ulcers associated with these conditions see Stasis Ulcer Chap XVI)

Ulcer Associated with Chronic Indurated Cellulitis Since areas of chronic indurated cellulitis (p 280) are potentially sites of lowered resistance even mild trauma to them may be sufficient to initiate an ulceration Such a lesion is resistant to therapy because of the underlying pathology The location of the ulcer in an area of brawny induration the presence of chronic venous stasis and the absence of impairment of arterial circulation should help make the proper diagnosis

ULCERATION OF NONVASCULAR ORIGIN

There are a number of unrelated nonvascular entities in which ulceration of the extremities may be present either as part of the clinical picture or as a complication (Table 10) It is therefore necessary to consider at least the following possibilities in the differential diagnosis of such a finding blood dyscrasias diseases with neurotrophic changes conditions associated with ulcerating subcutaneous nodules cardiovascular disorders chronic systemic infections like syphilis and tuberculosis acute infectious processes and cutaneous malignant tumors Some of these will be discussed below

Ulcers Associated with Blood Dyscrasias

Sickle Cell Anemia Ulcers of the legs are relatively common findings in this condition [illegible] being more likely to develop [illegible] There may [illegible] site being [illegible] (Fig 9B) [illegible] in appearance and may show pigmentation and cicatrization Although healing may occur after such therapy as the

Disorders in which Lesion is Found An ischemic ulcer may be part of the clinical picture of any of the occlusive arterial vascular disorders Most commonly however, it is found in arteriosclerosis obliterans and thromboangiitis obliterans A differential point between the two is the fact that in the latter the nutritional disturbance may be present both in the upper and lower extremities while in arteriosclerosis obliterans it is limited to the leg and foot Otherwise, there is no significant difference between the two types of lesions and hence it is necessary to utilize other criteria to make the proper diagnosis (p 137 and Table 13 p 140)

Scleroderma may also manifest ulcer formation Generally the lesion is shallow and not associated with much pain The presence of the thickened firmly adherent skin the loss of the normal wrinkling observed over the joints of the digits, the absence of venous stasis and of organic changes in the main arteries to the limb and the location of the lesion in the tips of the fingers all serve to differentiate it from trophic disturbances produced by other types of vascular disorders The poor response to most therapeutic procedures is also of diagnostic import

Other organic arterial vascular disorders in which ischemic ulcers may occur are Leriche s syndrome, in which there is a slow thrombosis of the aorta at its bifurcation, and trauma to main arterial channels necessitating ligation or resulting in *the formation of an arteriovenous aneurysm* The *differential diagnosis* of these conditions should in most instances offer little difficulty provided an adequate history is obtained and the physical findings are carefully interpreted

Functional Arterial Vascular Disorders

Although by definition functional vasospastic disease are entities in which there is only temporary and entirely reversible occlusion of arteries in the long standing severe cases pathologic changes may occur in the terminal branches which are conducive to the formation of small digital ulcerations An example of this type of change may be noted in Raynaud s disease, in which *the lesion is* generally limited to the distal portion of the digits and is quite superficial (Fig 10 p 114) The history of the typical color change in the involved digits and the absence of structural abnormalities in the main vessels *to* the limb are of value in differentiating the ulceration of Raynaud s disease from that due to an occlusive arterial vascular disorder (For further details see *Nutritional disturbances* of Raynaud s disease Chap VIII)

Ulceration of Venous Origin

The most common cause of ulcers of the lower extremity is venous stasis secondary either to pooling and stagnation of blood in varicose veins or to incompetency of the deep venous system The lesion is generally found on the medial aspect of the ankle and less often on the lateral side Rarely is it present above the mid portion of the leg (Table 10)

Ulcer of Postphlebitic Syndrome The ulceration which appears as a sequel to acute deep thrombophlebitis of the lower extremity may start with either necrosis and separation of the superficial layers of the skin or a portion of the wall of the vein may slough away together with the overlying tissues Almost

invariably the process penetrates the deep fascia The result is an irregularly shaped painful trophic disturbance varying in size from a pinhead to a lesion covering a considerable portion of the leg (Fig 38A p 282) The base is usually covered by a dirty exudate from which different types of organisms may be cultured A concomitant foul odor is a common finding The surrounding area is generally scaly indurated swollen markedly pigmented and has a purplish hue when the limb is in dependency There may be a secondary infection which is manifested by signs of inflammation around the ulcer

Varicose Ulcer The ulceration due to primary varicosities may resemble that which follows deep thrombophlebitis and at times it is difficult to differentiate between the two However the former is usually more superficial rarely penetrating the deep fascia and less resistant to therapy (Fig 38B and C pp 283 and 284) Furthermore no history can be elicited of an acute episode of marked swelling of the limb associated with systemic responses as is present in the case of deep thrombophlebitis At times it may be necessary to resort to venography and venous pressure measurements with exercise (p 406) to determine whether or not a block exists in the deep venous system The demonstration of a regurgitant flow in the superficial vessels is of no value as a differential point since this situation may be present both in varicosities secondary to incompetency of the deep venous system and in the primary type (For the treatment of ulcers associated with these conditions see *Stasis Ulcer* Chap XVI)

Ulcer Associated with Chronic Indurated Cellulitis Since areas of chronic indurated cellulitis (p 280) are potentially sites of lowered resistance even mild trauma to them may be sufficient to initiate an ulceration Such a lesion is resistant to therapy because of the underlying pathology The location of the ulcer in an area of brawny induration the presence of chronic venous stasis and the absence of impairment of arterial circulation should help make the proper diagnosis

ULCERATION OF NONVASCULAR ORIGIN

There are a number of unrelated nonvascular entities in which ulceration of the extremities may be present either as part of the clinical picture or as a complication (Table 10) It is therefore necessary to consider at least the following possibilities in the differential diagnosis of such a finding blood dyscrasias diseases with neurotrophic changes conditions associated with ulcerating subcutaneous nodules cardiovascular *disorders* chronic systemic infections like syphilis and tuberculosis acute infectious processes and cutaneous malignant tumors Some of these will be discussed below

Ulcers Associated with Blood Dyscrasias

Sickle Cell *Anemia* Ulcers of the legs are relatively common findings in this condition[1] being more likely to develop in adults than in children There may be multiple or single lesions on one or both lower extremities the usual site being about the ankle or on the lower half of the anterior surface of the leg (Fig 9B) The ulcer is typically punched out in appearance and may show pigmentation and cicatrization Although healing may occur after such therapy as the

use of ointments, bed rest and elevation, pressure dressings sympathectomy, and excision and grafting recurrence will generally take place The presence of a chronic ulcer on the leg of a Negro and the findings of sickling in the peripheral blood, slightly jaundiced sclerae, hematomegaly, splenomegaly and arthralgias in the absence of any impairment in local arterial or venous circulation, support the diagnosis of sickle cell anemia

Neurotrophic Ulcers

Perforating ulcers of the foot may occur in a number of unrelated neurologic conditions, such as peripheral neuritis from various causes, cord lesions tabes, and syringomyelia The trophic change may be noted under the metatarsal of the great toe on the sides of the foot, and occasionally on the dorsum It generally starts as a callus under which there is suppuration The ulceration enlarges progressively, affecting tendons, and later bones and sometimes even joints Despite the marked destruction of tissues, pain is usually minimal All these characteristics, associated with a normal local arterial and venous circulation and an underlying neurologic state, should help in the differential diagnosis of the neurotrophic ulcer

Ulceration of Subcutaneous Nodules

There are a number of nonvascular conditions associated with the formation of subcutaneous nodules which subsequently break down and ulcerate An example of this type of change is the degeneration that may occur in a syphilitic gumma (Fig 9C) Such a lesion is usually found on the leg and occasionally on the thigh Most often it is symptomless, although it may become painful if it is secondarily infected When healing occurs the site of the ulcer is first pigmented but later it gives the appearance of being centrally blanched

The presence of a positive serology the marked therapeutic response to anti luetic treatment, and the absence of improvement with procedures ordinarily used for trophic disturbances of venous origin help to differentiate the syphilitic ulcer from others Lesions which should especially be considered in the differential diagnosis are the ulcerations of subcutaneous nodules found in erythema induratum and chronic pernio (Fig 50 p 332) Both types generally appear on the lower third of the leg or over the calf and frequently are associated with pain In chronic pernio the relationship between the appearance of the ulcers and the onset of winter is also of significance, while in erythema induratum, there may be findings of tuberculosis elsewhere

Ulcers Due to Other Local Causes

There are several other local conditions or states which are associated with ulcers of the extremities Among these are traumatic lesions which can develop despite the presence of a normal blood supply When financial compensation is at stake, the possibility of a factitious ulcer (Fig 9E) must always be considered This can mimic almost any type of disorder discussed in this section although physical examination reveals no possible etiologic factor It is also well to re

member that neoplasms of the skin such as an epithelioma melanoma, and fibrosarcoma may break down to form an ulcerative lesion

Ulcers Associated with Cardiovascular Disorders

Congestive Heart Failure with Edema Massive swelling of the lower extremities associated with congestive heart failure predisposes to the production of ulcers of the leg As a result of marked stretching of the skin by edema fluid the resistance of tissues to infection is lowered Frequently a coexisting eczema is responsible for scratching which provides the mechanism necessary to permit bacteria to enter the skin and subcutaneous tissues and thus initiate the lesion Generally the ulcer is shallow and is located on the lower portion of the leg (Fig 9D) The presence of bilateral pitting edema and of signs of impairment of cardiac reserve elsewhere is of importance in differentiating this type of lesion from those produced by a peripheral vascular disorder The rapidity with which healing occurs with the removal of the edema and the use of some tissue stimulating ointment is also of diagnostic value Since palpation of the peripheral pulses is difficult because of the swelling oscillometry must be utilized in determining the state of the local arterial blood flow However it is necessary to point out that the readings may be somewhat reduced not because of any structural changes in the blood vessels but because of impairment in cardiac function

Hypertension A clinical syndrome has been described in which ulcers of the legs are associated with hypertension. The lesions appear spontaneously and are generally located on or above the lateral malleolus They are superficial indolent and quite painful In a female the combination of hypertension and an ischemic appearing ulcer on the leg in the absence of signs of impairment of arterial or venous circulation should help make the diagnosis However certain entities such as syphilis polycythemia rubra vera ulcerative colitis and cutaneous sensitivity to drugs must first be ruled out as possible etiologic agents

GANGRENE

As in the case of ulceration the presence of a gangrenous lesion in an extremity indicates that the amount of nutrition reaching the tissues locally is inadequate for their resting metabolic needs (Table 11) However the impairment generally is of a greater degree thus producing irreversible changes Not infrequently gangrene and ulceration coexist the latter accelerating the rate of destruction of tissue Whereas the basis for ulceration is not necessarily vascular gangrene is almost invariably associated with a marked reduction in local arterial blood flow

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[illegible] to the skin which is not altered by digital pressure (p 9) At this stage the tissues may appear distended with fluid and almost fluctuant particularly if the process is located in the distal portion of a digit

Dry Gangrene If there is no superimposed infection then absorption of fluid will occur producing mummification of the tissues (Fig 20 p 164) This

Table 10 Differential Diagnosis of Ulceration in the Extremities

Clinical entities in which lesion is found	*Underlying mechanism*	*Initiating factor*	*Location of lesion*	*Description of lesion*	*Type and severity of pain*	*Signs of impairment of local circulation*	*Prognosis*
Sequel of deep thrombophlebitis (postphlebitic syndrome)	Venous stasis	Insect bite scratch slight trauma	Inner aspect of lower third of leg near medial malleolus	Large odorous deep irregular crater covered with necrotic tissue & associated with secondary infection	Severe pain in site tenderness in surrounding tissues	Vasospasm may be present signs of venous stasis invariably present	Poor with regard to permanent healing
Varicosities acquired & congenital arteriovenous fistula	Venous stasis	Insect bite scratch slight trauma	Inner aspect of lower third of leg above foot in case of a v fistula distal part of foot	Superficial ulceration may be infected or clean	Fairly severe pain in site	Signs of incompetency of valves in superficial veins signs associated with a v fistula	Good with combined medical & surgical approach
Chronic indurated cellulitis	Venous stasis and chronic inflammation	Trauma	Leg	Superficial ulcer in a base of brawny induration	Pain present	Signs of venous stasis	Good if chronic cellulitis can be controlled
Arteriosclerosis obliterans & thromboangiitis obliterans	Chronic anoxia of skin	Trauma to area at times no precipitating factor	Generally toes dorsum of foot and heel less frequently fingers legs	Small or large lesions superficial or deep secondary infection may be present also necrotic eschar	Generally quite severe particularly in case of thromboangiitis obliterans	Signs of marked impairment of arterial circulation	Poor for the most part although healing may occur with medical therapy and sympathectomy

Table 10 (continued)

Clinical entities in which lesion is found	*Underlying mechanism*	*Initiating factor*	*Location of lesion*	*Description of lesion*	*Type and severity of pain*	*Signs of impairment of local circulation*	*Prognosis*
Raynaud s disease	Repeated attacks of transient acute anoxia	Slight trauma pin prick	Tips of fingers	Small superficial ulceration may have some serum or necrotic eschar covering it may be secondarily infected	Generally severe out of proportion to size of lesion	No signs of impairment of main arterial system	Good with medical or surgical treatment
Sclerodactylia	*Compression* of cutaneous vessels by scleroderma tous process	*Slight* trauma	Tips *of* fingers	Small shallow indolent ulcers	*Generally* not severe	No signs of impairment of main arterial system	Generally poor
Chronic pernio and erythema induratum	Angiitis of small ves sels in skin panniculitis	Spontaneous ulceration of nodules	Legs lower two thirds	Breakdown of *superficial* nodule-ragged *undermined* edge shallow ulcer	*Lesion quite painful*	*No signs of* impairment of arterial or venous *circulation*	Generally poor
Local injury	Destruction of skin and subcutaneous tissue by *trauma*	Trauma of *skin*	Sites exposed to trauma	Variable size and depth depending on severity of injury	Pain generally present	No signs of impairment of arterial or venous circulation	Good unless lesion is widespread
Nonspecific low grade skin infection pyogenic or fungus infection	Chronic inflammation	*Trauma*	Leg	Nonspecific	Variable	No signs of arterial or venous *insufficiency*	Good

Table 10 Differential Diagnosis of Ulceration in the Extremities

Clinical entities in which lesion is found	*Underlying mechanism*	*Initiating factor*	*Location of lesion*	*Description of lesion*	*Type and severity of pain*	*Signs of impairment of local circulation*	*Prognosis*
Sequel of deep thrombophlebitis (postphlebitic syndrome)	Venous stasis	Insect bite scratch slight trauma	Inner aspect of lower third of leg near medial malleolus	Large, odorous deep irregular crater covered with necrotic tissue & associated with secondary infection	Severe pain in site tenderness in surrounding tissues	Vasospasm may be present signs of venous stasis invariably present	Poor with regard to permanent healing
Varicosities acquired & congenital arteriovenous fistula	Venous stasis	Insect bite scratch slight trauma	Inner aspect of lower third of leg above foot in case of a v fistula *distal* part of foot	Superficial ulceration may be infected or clean	Fairly severe pain in site	Signs of incompetency of valves in superficial veins signs associated with a v *fistula*	Good with combined medical & surgical approach
Chronic indurated *cellulitis*	Venous stasis and chronic *inflammation*	Trauma	Leg	Superficial ulcer in a base of brawny induration	Pain present	Signs of venous stasis	Good if chronic cellulitis can be controlled
Arteriosclerosis obliterans & thromboangiitis obliterans	Chronic anoxia of skin	Trauma to area at times no precipitating factor	Generally toes dorsum of foot and heel less frequently fingers legs	Small or large lesions superficial or deep secondary infection may be present *also necrotic* eschar	Generally quite severe particularly in case of thromboangiitis obliterans	Signs of marked impairment of arterial circulation	Poor for the most part although healing may occur with medical therapy and sympathectomy

stage has been called dry gangrene Little or no odor is present Gradually the superficial layers become dry and brittle the same process taking place in the deeper structures as in the bone A clear-cut line of demarcation may be noted between dead and living tissues Signs of tissue reaction during the entire process are minimal and are limited to the site itself Little or no secretion is observed on the surface although surgical penetration of the gangrenous material generally reveals some liquefaction in the interior

Wet Gangrene If the lesion becomes secondarily infected then the course of events is somewhat different Inflammation generally occurs at the borders of the dead material and may penetrate some distance into normal structures Lymphangitis may also be associated with the spread of this process The dry appearance of the lesion is lost to be replaced by a stage of wet gangrene due to the breakdown of the necrotic structures by bacterial action and the production of pus An odor of decaying tissue is generally associated with this type of change The degree of pain may be considerable depending upon the rate of extension of the gangrenous process into adjoining normal regions The progress of the condition is enhanced by the formation of thrombi in the neighboring small blood vessels the response ultimately leading to complete occlusion and further local anoxia The vascular changes are frequently initiated by the inflammatory state of the tissues through which the vessels pass

Site of Lesion As in the case of the ischemic ulcer gangrene generally occurs in the distal portions of the extremities the digits and the heel since such sites are furthest removed from the source of blood supply and hence suffer the most from any existing anoxia Even the slightest injury to them may therefore be enough to initiate a nutritional disturbance Trauma to the leg or forearm where the local circulation would be expected to be relatively more adequate may have the same effect if the lesion is extensive enough

Factors Producing Gangrene

Irreversible Changes in Main Arteries

Spontaneous Onset of Gangrene Irreversible and progressive structural alterations in the walls of main arteries or their subdivision may eventually produce enough ischemia of tissues to lead to gangrene Such pathologic changes occur in thromboangiitis obliterans arteriosclerosis obliterans polyarteritis nodosa and other generalized vascular conditions (Fig 26 p 185) Where local circulation has been greatly reduced through occlusion of a main artery by an embolus (Fig 18 p 150) or thrombus (Fig 22 p 169) or by ligation of a traumatized vessel gangrene of the distal portion of the involved limb may also take place

Factors Precipitating Gangrene Aside from a gradually increasing state of anoxia due to the natural advancement of the obliterative process there are several other factors which may initiate gangrene even in an extremity with only a mild to moderate impairment in blood supply Most potent among these is the local application of heat (p 457 and Fig 19 p 159) Prolonged exposure to moderate cold of a degree which would ordinarily have no deleterious effect on the normal individual may likewise be sufficient to produce nutritional dis

Table 10 (continued)

Clinical entities in which lesion is found	*Underlying mechanism*	*Initiating factor*	*Location of lesion*	*Description of lesion*	*Type and severity of pain*	*Signs of impairment of local circulation*	*Prognosis*
Peripheral neuritis cord lesions tabes and syringomyelia	Hypesthesia and anesthesia	Spontaneous or associated with trauma	Base of great toe side or dorsum of foot	Penetrating ulcer beneath a callus widespread involving skin and underlying tissues (neurotrophic ulcer)	For the most part lesion is painless	No signs of impairment of arterial or venous circulation	May be good if specific therapy is available poor if due to destruction of cord
Sickle cell anemia	Stasis of blood thrombosis of small vessels with anoxia of skin	Spontaneous or after mild trauma	Ankle and lower portion of anterior surface of leg	Punched out appearance indolent may be secondarily infected pigmentation and cicatrization may be present	Painless	No signs of impairment of arterial or venous circulation	Poor recurrences after healing
Syphilis	Breakdown of a gumma	Spontaneous or due to trauma	Upper half of leg less often on thigh	Round or oval sharply defined border giving punched out appearance surrounding skin shows purplish pigmentation	Almost always painless	No signs of impairment of arterial or venous circulation	Good with specific therapy
Congestive heart failure with marked edema	Anoxia of skin due to stretching by edema fluid	Scratching slight trauma	Lower third of leg	Superficial ulcer of variable size may be secondarily infected	Pain may be moderate	Pulsations may be difficult to feel because of edema	Good if edema can be controlled

Table 11 *Differential Diagnosis of Gangrene in the Extremities*

Clinical entities in which lesion is found	*Underlying mechanism causing impairment of cutaneous circulation*	*Location and description of lesion*	*Associated pain*	*Signs of impairment of local circulation*	*Prognosis*
Thromboangiitis obliterans	Structural changes in main arteries trauma may be a precipitating factor	Foot fingers & legs less frequently involved local inflammation generally not present dry type of gangrene	Generally severe con stant pain at times excruciating	Impaired arterial circulation of feet & legs invariably present similar changes present in upper extremities if involvement is in hands	Outlook good if lesion is limited to digits if extension occurs onto adjoining portion of foot or hand possibility of preserving extremity is poor better prognosis for upper extremity
Senile type of arteriosclerosis obliterans	Structural changes in main arteries trauma may be a precipitating factor	Foot leg less often involved local inflammation infrequently present dry type of gangrene	Moderately severe constant pain at times symptoms may be minimal	Impaired arterial circulation of feet and legs invariably present	Outlook good if lesion is limited to toes if extension occurs onto adjoining portion of foot extremity will probably have to be sacrificed
Arteriosclerosis obliterans associated with diabetes mellitus	Structural changes in main arteries infection plays a definite role trauma may be a precipitating factor	Foot leg less frequently involved local inflammation almost invariably present at times lymphangitis generally wet type of gangrene	Moderately severe con stant pain at times symptoms may be minimal	Impaired arterial circulation of feet invariably present	Outlook good if lesion is limited to toes and if local infection can be controlled if extension occurs onto adjoining portion of foot extremity will probably have to be sacrificed
Occlusion of main artery by thrombus or embolus or ligation of traumatized vessel	Absence of blood flow through main artery and a superimposed vasospasm	Foot leg less frequently rarely the hand generally dry type of gangrene very little inflammation	Generally severe constant pain	Impaired arterial circulation invariably present	Outlook generally poor and part of extremity will probably have to be sacrificed

turbances when an already precarious cutaneous circulation exists (p 458 and Fig 14B, p 134) If a patient with an occlusive arterial disease but with no gangrene develops a deep thrombophlebitis, the additive effect of distension of structures by edema fluid may now be enough to precipitate death of tissues in the digits The same result may follow forced extension of the limb with a reduced circulation as in the treatment of an orthopedic condition Therefore, it cannot be emphasized too strongly that in the presence of an impaired blood supply, vigilance must be exercised at all times, in order to prevent gangrene

Thrombosis of Small Arteries

In certain instances, gangrene of a portion or an entire digit may occur as a result of thrombosis of the digital artery or its branches Under these circumstances the circulation through the main arterial tree or in the other uninvolved digits is generally normal An example of this type of response is the superficial gangrene associated with an acute infectious disease like typhus fever, typhoid fever pneumonia or trichinosis (Fig 20A, p 164)

Spasm and Secondary Thrombosis

Gangrene may occur in extremities with previously normal arteries as a result of marked spasm, followed by secondary thrombosis Such an alteration is noted in the limb exposed to a low environmental temperature with or without the factor of moisture (Figs 45, 48 and 49 pp 321, 327 and 328) The anoxia and subsequent death of tissues are due to involvement of the small arteries locally Prolonged or repeated short periods of spasm of large arteries and their branches may produce similar changes in these vessels Typical of such a reaction is the occasional case of gangrene of the fingers observed in a patient with the scalenus anticus cervical rib, or hyperabduction syndrome as a result of thrombosis of the subclavian artery Finally, at times forced extension even in the extremity with a normal blood supply may cause sufficient spasm of vessels and reduction in local circulation to initiate irreversible trophic disturbances

Mechanical Obstruction

Gangrene may also be noted in instances in which a normal arterial vascular tree is compressed by mechanical factors to the point of preventing adequate nutrition from reaching the tissues For example in certain cases of deep thrombophlebitis in which there is marked stretching of tissues by the considerable edema fluid (phlegmasia cerulea dolens p 247, the arterial blood supply to the toes may be so reduced as to result in loss of viability of tissues and the production of gangrene (Fig 32C, p 246)

At times extravasation of blood into the cutaneous and subcutaneous tissues of a distal portion of a digit may be followed by loss of viability of the tip despite the existence of a normal circulation in the main arterial channels Such a response may be noted in certain blood dyscrasias The result is generally the production of superficial gangrene of the involved portion and rarely the loss of a part of the

Table 11 (continued)

Clinical entities in which lesion is found	*Underlying mechanism causing impairment of cutaneous circulation*	*Location and description of lesion*	*Associated pain*	*Signs of impairment of local circulation*	*Prognosis*
Acute infectious diseases	Thrombosis of digital arteries	Fingers and toes generally dry gangrene and no inflammation	Moderate to severe con stant pain	No signs of involve- ment of main ar- terial channels	Outlook good for extrem ity but not for involved digit or digits
Scalenus anticus or cervical rib syndrome	Slow thrombotic process in subclavian artery due to pressure	Tips of fingers	Moderate pain	Reduction in pulsa- tions & oscillo- metric readings	Outlook good for extremity

Table 11 (continued)

Clinical entities in which lesion is found	*Underlying mechanism causing impairment of cutaneous circulation*	*Location and description of lesion*	*Associated pain*	*Signs of impairment of local circulation*	*Prognosis*
Polyarteritis nodosa and other generalized vascular disorders	Thrombosis of small arterial channels	Portions of digits of hand or foot or entire digit ' dry ' type of gangrene no inflammation	Moderately severe constant pain	No signs of involvement of the main arterial channels	Outlook good for the local lesion
Frostbite trench foot and immersion foot	Marked vasospasm and thrombosis of small arteries	Digits of foot or hand dry or wet gangrene	Moderately severe pain	No signs of involvement of main arterial channels	Outlook good for the extremity but poor for the involved portions unless superficial gangrene is present
Raynaud s disease	Repeated periods of acute anoxia associated with thrombosis of terminal branches of digital artery	Tips of fingers and infrequently of toes small areas of gangrene with superimposed inflammation	Very severe pain initiated even by pressure of bandage	No signs of involvement of main arterial channels	Outlook good for preservation of digit although tip may be lost
Sclerodactylia	Strangulation of local blood flow by sclerodermatous process	Tips of fingers small areas of necrosis generally without inflammation	Mild to moderate pain	No signs of involvement of main arterial channels	Outlook poor since process continues to progress
Severe degree of acute deep thrombophlebitis	Marked interference with venous return pressure necrosis vasospasm	Toes and at times portions of the legs dry type of gangrene	Severe pain	Classical findings of thrombosis of iliofemoral vein vasospasm may also be present	Outlook good for extremity but not for involved sites

PART TWO

PERIPHERAL VASCULAR DISEASES

digit It is possible that a contributing factor is an associated thrombosis of the small arterial channels, related to changes in blood constituents

Finally, the effect of mechanical factors can be noted in sclerodactylia, where superficial gangrene of the involved digits is a not uncommon complication In this condition there is again no impairment in the main arterial tree, the underlying mechanism for the local ischemic state being gradual strangulation of the superficial capillaries by the sclerodermatous process

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CHAPTER

VIII VASCULAR ENTITIES PRIMARILY AFFECTING THE ARTERIAL TREE

I CLASSIFICATION, RAYNAUD'S DISEASE

CLASSIFICATION

Since our present state of knowledge does not permit the formation of a completely satisfactory classification of peripheral vascular disorders all that can be achieved in the case of arterial vascular diseases is the establishment of two subdivisions the functional and the occlusive types

Functional Arterial Vascular Disorders The clinical entities falling into this group are characterized by temporary and generally reversible alterations in local blood flow due to transient changes in vasomotor control over the various components of the arterial system Pathologic abnormalities are usually not present in the walls of the involved vessels unless the process is long lasting or extremely severe

Functional arterial vascular disorders can be divided into two categories depending upon whether vasoconstriction or vasodilatation is the predominant response Examples of vasospastic states are Raynaud's disease Raynaud's syndrome acrocyanosis livedo reticularis and causalgia Vasospasm may also be present in a number of unrelated nonvascular entities Purely vasodilator conditions are represented by erythromelalgia There are also diseases in which both vasospasm and vasodilatation are present but in different periods of the clinical course Typical of such entities are trench foot immersion foot frostbite and posttraumatic vasomotor disorders

Occlusive Arterial Vascular Disorders This second subdivision of arterial diseases consists of those conditions in which a permanent and irreversible reduction in peripheral blood flow exists It differs from the category of functional vascular diseases in the consistent presence of pathologic changes in the walls of the arteries which lead to narrowing or complete obstruction of the lumen The process may occur either slowly or rapidly Examples of chronic occlusive disorders are thromboangiitis obliterans arteriosclerosis obliterans and several much less common conditions including polyarteritis nodosa scleroderma dermatomyositis and disseminated lupus erythematosus The more acute type of

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Pathogenesis

Basis for Color Change Pallor the typical initial color change in Raynaud's disease is due to spasm or functional obliteration of the digital arteries supplying the fingers and toes Because there is a resulting absence of arterial inflow during the attack the cutaneous vessels soon become empty of blood and blanching ensues Although the arterioles capillaries and venules are considered only passively involved in this reaction it is possible that the existing anoxia produces active spasm of the minute vessels of the skin thus contributing to the characteristic waxy pallor Despite such changes in the arterial tree locally the pulse at the wrist or in the foot never disappears although it may become smaller

Several explanations have been offered for the appearance of cyanosis In one it is postulated that spasm of the digital artery is intermittently released in the attack, permitting blood to enter the capillaries at a very slow rate This results in stasis in the minute cutaneous vessels and the removal of a greater than normal quantity of oxygen from each unit of blood As a consequence of the accumulation of reduced hemoglobin in the subpapillary venous plexus the skin is colored blue Another possibility is that blood is trapped in the superficial vessels during the period of arterial spasm It has also been suggested that there is an associated venospasm in Raynaud's disease which if predominant will cause stasis in the digits again furthering the loss of oxygen from the blood In the absence of arterial spasm it is believed that venospasm may produce cyanosis and even swelling while pallor will be absent [18]

On removal of the spasm of the digital vessels as by exposure to warmth there is a rapid dilatation of the arterioles capillaries and venules and a resumption of local circulation With the entrance of normally oxygenated arterial blood into the vessels at an increased rate the skin displays a rubor This reaction can be considered to be a manifestation of reactive hyperemia (p 468) an attempt to repay the blood flow debt incurred during the previous period of obliterated circulation As complete recovery occurs the skin assumes its normal tint

Basis for Digital Spasm Considerable controversy exists regarding the mechanism that initiates spasm of the digital arteries It is the opinion of some workers [10] that the abnormality is in the sympathetic innervation of these vessels while others [1, 2, 15] believe that the arteries themselves possess an inherent increased sensitivity to cold In support of the latter view is the finding that after complete sympathetic denervation as through *sympathectomy* direct application of cold to the digits still elicits a definite though reduced response Most of the other available evidence is also in favor of the conclusion that in Raynaud's disease there is a constitutional change *in the walls of the blood* vessels which makes them react abnormally to normal vasoconstrictor impulses and to circulating epinephrine Involvement of the sympathetic nerves however cannot be entirely excluded

Morbid Anatomy

Changes in Digital Arteries Although Raynaud's disease is generally not associated with pathologic alterations in the walls of the *digital arteries* if the process is advanced or is of a degree sufficient to produce *nutritional* disturbances intimal hyperplasia and fibrosing medial changes may be found which reduce the

occlusion is represented by such clinical entities as embolism and sudden thrombosis of a main artery. Arterial and arteriovenous aneurysms and laceration or severance of a large arterial channel also fall into this group. Some of the above entities may manifest a superimposed state of vasospasm which causes exaggeration of the existing anoxia of tissues.

The following discussion of conditions affecting the arterial tree does not conform exactly to the plan already outlined. For example, all functional vascular disorders except Raynaud's disease have been removed from their proper position in the classification and discussed briefly in a chapter devoted to rare vascular entities (Chap. XXI), since such pathologic states are infrequently encountered by the general practitioner. Furthermore, because of a common etiologic basis, it has been felt advisable to take out of this section those arterial disorders produced by injury, whether functional or occlusive in type, and group them elsewhere (Chaps. XVII-XX inclusive).

RAYNAUD'S DISEASE

Of all functional or vasospastic disorders, Raynaud's disease is perhaps the best known. It was first described as a clinical entity in 1862,[18] but since then wide divergence of opinion has been expressed in the literature as to the clinical findings necessary for the establishment of such a diagnosis. Some workers have grouped loosely under this designation a variety of circulatory disorders, all of which have as a prominent feature an abnormal responsiveness to cold. Others, however, believe that the term should be reserved only for those cases in which the clinical picture satisfies in all regards certain criteria.[3] Since the latter view has much in its favor, it will be followed in this presentation.

Raynaud's disease is a clinical entity which is characterized by intermittent color changes in the fingers and toes elicited by exposure to cold or emotional excitation. Typically, a triphasic alteration is noted, consisting of pallor (digital syncope) (Fig. 2A, p. 28), cyanosis, and rubor in that order, and then the return to a normal color. However, there may be several variations. The attack may be ushered in by the appearance of cyanosis while pallor may be absent, or the latter may be followed by rubor without cyanosis intervening. In some instances rubor may not be noted, with pallor or cyanosis being replaced by normal color. However, either pallor or cyanosis should be present during the entire period that the exciting stimulus acts.

Among other important points in diagnosis is the fact that no etiology for the disorder must be uncovered, for otherwise it falls into the category of Raynaud's syndrome (see p. 115) rather than Raynaud's disease. Furthermore, the attacks of color changes should have been noted for at least two years without signs or symptoms of an occlusive arterial vascular disorder. It is necessary to point out that although the condition is seen predominantly in young women, in a ratio of about 5 to 1, a typical color change in young men that conforms to the above criteria also warrants a diagnosis of Raynaud's disease.[1,9] Still, in general, it is advisable to consider such a finding in a male as a manifestation of Raynaud's syndrome associated with an occlusive arterial vascular disorder like thromboangiitis obliterans, until conclusively proved to be otherwise.

phalanges or even in all three However the process does not extend onto the rest of the hand or foot One or more fingers or toes may be affected simultaneously but infrequently the thumbs alone In fact, in most instances the latter are spared Although bilateral distribution with symmetrical digital involvement has been considered one of the criteria in the diagnosis of the condition unilateral color changes may be observed, especially early in the disease However if the alterations continue to be limited to one finger or one limb the possibility should be considered that they are due to some local etiologic agent such as pressure on vascular structures by an hypertrophied scalenus anticus muscle or by a cervical rib It is of interest that the digits of the hand are much more commonly affected than those of the foot and that when the process is present in both it is frequently more severe in the fingers

Other Physical Findings Aside from the color change the signs associated with Raynaud's disease are minimal In some patients slight swelling of the involved digits may occur during the attack and in others this may persist for some time after the skin has become normal in appearance Between episodes a mild degree of cyanosis and a lowered cutaneous temperature may persist, although with continuous exposure to a warm room such findings are generally not apparent Pulsations at the wrist and in the foot are usually normal or slightly reduced while the various tests for arterial insufficiency ordinarily reveal an unimpaired local blood flow However in the more severe case the digits may demonstrate the various trophic changes discussed below

Nutritional Disturbances Mild trophic changes in the involved digits are common in Raynaud's disease while those of serious import are rare The minor alterations may include an abnormal growth or brittleness of the nails with a widening of the cuticle (Fig 1C p 26) and thickening of the skin over the tips of the digits with or without repeated desquamation Later the subcutaneous tissue is lost this being manifested by prolonged dimpling of the skin after application of pressure to the fleshy portion of the finger There may be small calcium deposits in the subcutaneous tissue of the fingertips which can be observed on x ray If extensive they may be apparent through the skin Recurrent infections around the nails are a fairly common finding

Of a more severe nature are such nutritional changes as atrophic arthritis characterized by destruction of joint surfaces and deformities and sclerodermatous alterations The latter develop in about 10 per cent of cases of Raynaud's disease and are limited to the digits affected by the color episodes (sclerodactylia) When present the process may intensify the existing ischemia and thus predispose to gangrene of the fingertips Evidently the sclerodermatous changes in the skin act as constricting bands which mechanically interfere with the flow of blood through the smaller vessels of the fingers [17]

The most serious type of nutritional disturbance noted in Raynaud's disease is ulceration and superficial gangrene of the fingers Infrequently the process may appear shortly after the onset of the disorder but in most instances it is a complication of a long standing condition The extent of involvement is rarely as great as that observed in such obliterative vascular diseases as thromboangiitis obliterans or arteriosclerosis obliterans For the most part, the lesion is shallow and limited

lumen of the terminal branches.[14] In some instances actual occlusion may be present as a result of the ingrowth of cellular tissue or recent or organized thrombus. The clot may become recanalized, thus permitting the circulation to the distal portions of the digits to be resumed but precariously. Histologic studies have generally revealed no definite abnormalities of the sympathetic ganglia in Raynaud's disease.

Alterations in Capillary Bed. The appearance and behavior of the cutaneous capillaries in Raynaud's disease depend on the severity of the disorder. They also vary in the different color stages.[7] In the early and mild type the picture is not striking. The capillaries are tortuous, twisted and bent, with a spastic narrow arteriolar portion and a dilated, congested venular portion. The subpapillary venous plexus generally manifests congestion. In a severe case most of the capillaries are enlarged, some having a width of 5 to 8 red blood cell diameters, with a few even wider (giant capillaries). The vessel may be ringlike or hairpinlike or irregular and tortuous. Capillary flow is generally sluggish and prolonged stasis may be present. In some instances blood extravasates and thromboses may be noted.[7] If sclerodermatous changes coexist, there is also a reduction in the number of capillaries.

Clinical Characteristics

Although the definition of Raynaud's disease also includes an enumeration of the most important clinical characteristics of the disorder, it has been felt necessary in this section to elaborate upon some of the aspects mentioned and to present others to which no reference was made.

Symptoms

Certain symptoms may be associated with an episode of color change. Generally, during the period of pallor or cyanosis, the patient experiences a sense of coldness, numbness or tightness and at times an actual diminution of sensory acuity in the involved digits. In some instances, however, there may be no unpleasant sensations. As the attack wears off and the circulation is re-established, tingling, burning, throbbing or paresthesia may be experienced. Between episodes no symptoms are present except possibly a subjective sense of coldness in the hands and feet.

In the progressive type of Raynaud's disease the attacks may become more frequent and severe, being elicited by even slight reductions in environmental temperature or mild emotional strain. As a result, the condition may become almost disabling, since the patient will not be free of symptoms even during the warmer weather. It is in such a case that various nutritional disturbances are prone to develop.

Signs

Site of Involvement. The color change in Raynaud's disease is present in the digits, usually being noticed first in the tips and later in one or two distal

Differential Diagnosis

Raynaud's Syndrome (Raynaud's Phenomenon)

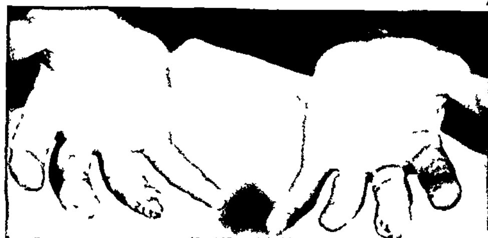
The main problem in the differential diagnosis of Raynaud's disease is to distinguish it from vascular and nonvascular entities that manifest typical episodes of color change in the digits initiated by exposure to cold or emotional excitation but do not satisfy in some regard the criteria previously enumerated. Such disorders are classified under the heading of Raynaud's syndrome. In this category is the condition called hereditary cold fingers, which occurs in young persons and is characterized by blanching, cyanosis and numbness of several digits on exposure to cold.[19] There is some question as to whether this entity is not a mild form of Raynaud's disease, although it is rarely progressive and may become less severe or disappear entirely.

Existence of an Underlying State or Disease. There are a variety of other entities in which typical color change occurs in the digits, but in each instance an etiologic agent can be established. Among these is pneumatic hammer disease, which results from the prolonged use of vibrating tools. Generally, when the patient takes on a new occupation, the episodes of color change disappear. A similar alteration may on occasion be observed in the fingers of typists or pianists. Mechanical interference with blood flow through main arteries as a result of external pressure may likewise produce periods of digital pallor. This type of response may be noted in cervical rib and scalenus anticus syndrome, in instances in which pressure is exerted in the axilla through the incorrect use of a crutch, and in the presence of compression of the brachial plexus and subclavian vessels by tumors.

Attacks of typical color change may be seen in a number of other conditions. Among these are the postfrostbite syndrome and certain organic neurologic diseases, as, for example, multiple sclerosis, tabes dorsalis and syringomyelia. Recently similar alterations have been reported in the presence of cold agglutinins complicating primary atypical pneumonia[5] and of cryoglobulins associated with multiple myeloma, leukemia and other disorders.[4, 11]

Collagen diseases. Raynaud's syndrome may also be noted in such disorders as scleroderma, polyarteritis nodosa, disseminated lupus erythematosus, dermatomyositis and rheumatoid arthritis. In the case of scleroderma the differential diagnosis may offer some difficulty, since the late stage of Raynaud's disease may be associated with sclerodermatous changes in the digits involved in the color episodes. It is therefore important in each instance to determine the sequence of events, i.e., whether the attacks of cyanosis or pallor began before or after the appearance of alterations in the consistency of the skin. In the case of Raynaud's disease color episodes generally exist for years before sclerodermatous changes are noted. Furthermore, when present, the latter are usually of a minor degree and are localized to the digits. On the other hand, in true scleroderma, Raynaud's syndrome is noted only as a late complication, and by then the alterations in the skin and subcutaneous tissue are prominent signs. Moreover, such abnormalities are found not only in the digits demonstrating color change but frequently also

to the ends of the digits (Fig 10A), although in the advanced stage it may be associated with bone destruction and absorption of the tips of the distal phalanges X ray examination may also show generalized decalcification of the bones Minute areas of gangrene may occur as a result of thrombosis of small vessels, the lesions usually leaving small depressed scars or pits at the fingertips



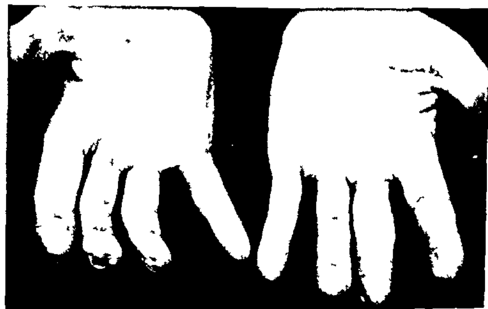


Fig 10 A Ulcers of fingertips occasionally observed in severe Raynaud s disease B Same hands several weeks after bilateral dorsal sympathectomy Lesions entirely healed leaving depressed scars

It is of interest that the excruciating burning sensation frequently associated with ulcers of the tips of the fingers is usually much out of proportion to the apparent severity of the trophic disturbances It may be that due to the loss of the upper layers of the skin the fine nerve endings are exposed with the result that even the weight of a simple bland ointment applied to the lesion may initiate marked symptoms

Table 12 (continued)

Clinical entity	*Pertinent points in history*	*Character and location of color changes*	*Structural changes in arterial system*	*Other abnormalities in limb*	*Underlying mechanism responsible for changes*
Sequelae of trench foot and frostbite	Prolonged exposure to low environmental temp and water	Constant uniform cyanosis of fingers and toes less often rest of foot	None	Hyperhidrosis frequently present	Constriction of cutaneous arterioles
Causalgia and posttraumatic vasomotor disorders	Trauma to extremity	Constant uniform cyanosis in involved hand or foot	None	Hyperhidrosis and edema may be present	Constriction of cutaneous arterioles
Syndrome of disuse	Maintaining extremity in dependency and immobile for prolonged period	Constant uniform cyanosis in involved hand or foot	None	Hyperhidrosis and edema frequently present	Constriction of cutaneous arterioles
Acute deep thrombophlebitis and postphlebitic syndrome	Pain in extremity associated with swelling fever malaise	Constant uniform cyanosis in involved foot and leg	None	Edema dilated or varicose superficial veins pigmentation	Spasm of large arteries at first and later spasm of arterioles
Rheumatoid arthritis & anterior poliomyelitis	Joint involvement or paralysis of muscles	Constant cyanosis in distal portion of involved limb	None	Coldness hyperhidrosis	Spasm of cutaneous arterioles

Table 12 Differential Diagnosis of Primary and Secondary Vasospastic States

Clinical entity	*Pertinent points in history*	*Character and location of color changes*	*Structural changes in arterial system*	*Other abnormalities in limb*	*Underlying mechanism responsible for changes*
Acrocyanosis	None	Constant uniform cyanosis located in entire hand & adjoining portion of forearm less often in foot and leg	None	Low skin temp	Arteriolar constriction and dilatation and paralysis of minute vessels of skin
Raynaud s disease	May be a history of abnormal responsiveness to cold	Pallor cyanosis & rubor limited to fingers and less often toes no involvement of rest of hand or foot changes episodic in type	None except in long-standing cases in which histologic changes may be present in small vessels no gross changes	Hyperhidrosis may be present marked variations in skin temp	Spasm of digital arteries
Livedo reticularis	None	Mottled reticular cyanosis constant located on legs and feet less often on forearms	None	Hyperhidrosis may be present	Spasm of minute cutaneous vessels
Vasospasm associated with occlusive vascular disorders	Intermittent claudication rest pain	Uniform diffuse cyanosis constant located in feet primarily Raynaud s syndrome limited to fingers toes	Gross changes invariably present	Hyperhidrosis may be present	Constriction of small arteries and arterioles structural changes in vessels also play a role

warmers used by sportsmen are quite effective in reducing the episodes of color changes the hands being kept in close contact with them during the entire period of exposure Mittens should be worn in preference to gloves because of their less constricting effect on the fingers A muff can be used by the female patient For the protection of the feet woolen socks and fur lined stadium boots or over shoes are useful Naturally, if at all practicable residence in a warm climate where the temperature is constant and dampness is slight is the most desirable way to cope with the problem

Protection from Trauma The patient must also exercise care in preventing trauma to the digits since even minor bruises or the prick of a pin may be sufficient to initiate superficial ulcers Duties which expose the hands to this danger should be eliminated

Sympathetic Blocking Agents An attempt to reduce attacks of color change by such drugs as Priscoline Hydergine and Dibenzyline is generally met with limited success but still this approach should be given a clinical trial All these substances cause temporary inhibition of vasomotor tonus and hence a decrease in responsiveness of the peripheral vessels to the stimulus of cold (For sites of action of sympathetic blocking agents see *Drugs Having an Inhibitory Action on the Sympathetic Nervous System* Chap XXV)

An adequate dose of Priscoline can only be determined by trial and error since there are marked individual variations in response to this drug A satisfactory plan is to have the patient start with 25 mg daily and increase the quantity up to the point of obtaining significant side effects and then maintain the dosage some what below this level In those instances in which Priscoline can be tolerated in sufficient quantity to have a definite blocking action it appears to reduce the severity and number of attacks of color changes

Hydergine has thus far had a limited clinical application in Raynaud's disease and hence any conclusions drawn are only tentative It is available in the form of a sublingual tablet (0 5 mg) which is taken several times a day The exact time interval for maximal protection of a specific patient and the size of the dose can again only be determined by trial and error The side effects from the drug with oral administration are minimal provided a single dose does not exceed 2 tablets There is some suggestive evidence that Hydergine reduces the severity of the color change and the associated pain

Dibenzyline is available in capsules of 10 15 and 25 mg and is generally taken several times a day Its effectiveness also varies from patient to patient The fact that it may not be tolerated by some individuals (p 497) somewhat limits its therapeutic value The clinical reports on the use of this drug in Raynaud's disease are at the moment insufficient for proper evaluation However from personal experience it appears to have some usefulness

Other Vasodilators Nicotinic acid by mouth has been tried in Raynaud's disease because of its known vasodilating action on the blood vessels in the hands The response occurs within 20–30 minutes after administration and lasts for about one half hour A trial dosage of 50 mg three times a day taken preferably before meals should be used initially and the quantity raised until the desired effect is produced With continued administration it may be necessary to increase

in the skin of the arms, face, chest, and neck (See *Differential Diagnosis of Chronic Occlusive Arterial Vascular Disorders*, Chap IX, for differentiation of Raynaud s phenomenon associated with these conditions from Raynaud s disease also Table 13 in the same chapter)

Vasospastic Diseases or States

Acrocyanosis Among the primary vasospastic disorders which may at times be mistaken for Raynaud s disease (Table 12) is acrocyanosis, since both conditions are characterized by color changes which appear primarily in young women However, in acrocyanosis episodes of typical color change are not noted nor is blanching ever present Instead the hands and to a lesser extent, the feet persistently demonstrate a diffuse cyanotic rubor which although being somewhat enhanced by exposure to cold, is not reduced or eliminated by a warm or hot environment Of further importance is the fact that the response is not limited to the digits in contrast to the findings in Raynaud s disease Moreover ulceration or superficial gangrene is never noted in this disorder

Livedo Reticularis Little difficulty should be encountered differentiating this condition from Raynaud s disease The reticular or blotchy appearance of the skin typical of the syndrome is constantly present and may involve the entire extremity Furthermore no episodic color change is noted in the digits (For further discussion of this condition as well as acrocyanosis see Chap XXI)

Vasospasm There are a number of conditions vascular and nonvascular in which vasospasm is a part of the clinical picture and which must be considered in the differential diagnosis of Raynaud s disease A typical finding in such disorders is that the hands and feet are usually cold this response being accentuated by a low environmental temperature At times the skin of one or more digits may be cyanotic or red, but a history of definite color change in sequence is not elicited The findings in this group are similar to those noted in normal individuals on exposure to cold the only difference being that the intensity of stimulus necessary to elicit the change is much less

Treatment

Since Raynaud s disease is a vasospastic disorder the therapeutic approach is aimed first at making the digital arteries less responsive to vasoconstricting stimuli through temporary or permanent elimination of sympathetic control over these vessels and second at reducing the possibility of initiating digital spasm by minimizing or neutralizing those factors which act as causative agents The appropriate procedures have been presented in two separate categories depending upon whether or not the patient is suffering from trophic disturbances

TREATMENT OF THE PATIENT WITH NO *NUTRITIONAL CHANGES*

Medical Therapy

Protection from Cold An important therapeutic measure is to decrease the periods of exposure of the body to cold to a minimum and to supply adequate covering of the extremities when in a cold environment The various types of hand

warmers used by sportsmen are quite effective in reducing the episodes of color changes the hands being kept in close contact with them during the entire period of exposure Mittens should be worn in preference to gloves because of their less constricting effect on the fingers A muff can be used by the female patient For the protection of the feet woolen socks and fur lined stadium boots or over shoes are useful Naturally, if at all practicable residence in a warm climate where the temperature is constant and dampness is slight, is the most desirable way to cope with the problem

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the amount since some tolerance is built up. The patient should be warned of the itching and prickly sensation of the face and the sense of warmth that follow adequate dosage. However, there are very few severe side reactions and hence the drug is worthy of a clinical trial.

Whisky and other alcoholic beverages also have a beneficial action because of their vasodilating effect on cutaneous blood vessels. In fact, a drink of whisky can be quite useful in counteracting a severe episode of color change which does not respond to exposure to a warm environment. The routine use of several ounces daily may help reduce attacks.

Nitroglycerine in a lanolin base (Nitrol ointment) has been found efficacious when used locally.[13] The ointment, containing 2% nitroglycerine (glyceryl trinitrate), is rubbed lightly into the skin of the involved digits three or four times a day, using a rubber glove to prevent absorption in the finger applying the medication. A reduction in the severity of the attacks of color change may be produced through a direct paralyzing effect on the musculature of the vessels in the digits. (For pharmacologic action of nitrites, see *Drugs Having a Direct Vasodilating Effect*, Chap. XXX.)

Psychotherapy. Every patient with Raynaud's disease should receive a certain amount of guidance in adjusting to her disability. She should be reassured of the fact that although it may cause her inconvenience and some pain and limit her period of exposure outdoors, it is by no means dangerous. Once the patient accepts such a point of view, in many instances the resulting lessening of tension helps reduce the severity and number of attacks.

Of course, if signs of a psychiatric disturbance are present, it is necessary to seek specialized care. Thereafter close cooperation between the practitioner and the psychiatrist is essential. Such an approach may reduce the attacks of color change brought on by emotional excitation. Sedation may also be utilized in reducing the patient's reactivity to all types of stimuli.

Abstinence from Smoking. There appears to be little question that this aim is desirable provided it can be accomplished without too much psychic trauma. Although an obvious correlation between smoking and the progression of the disorder as exists in the case of thromboangiitis obliterans (p. 193) can not be established for Raynaud's disease, in the latter condition the blood vessels are hyperresponsive to all types of vasoconstricting stimuli including smoking. If the patient can not abstain, she should at least not smoke when outdoors in the cold.

Surgical Therapy

Sympathectomy. Although opinion is by no means unanimous, the general feeling is veering to the view that sympathectomy plays only a limited role in the treatment of the patient with Raynaud's disease without nutritional disturbances. Certainly in the mild case such a heroic step is not warranted. Nor should the procedure be used in the individual who has widespread involvement—for example in all four extremities. Under such circumstances, sympathetic denervation would have to be so extensive in order to control the condition that there would result

a marked impairment in the mechanism of heat loss from the body through sweating. This unphysiologic state may be associated with definite untoward effects. (For further discussion of this point see *Role of the Sympathetic Nervous System in the Maintenance of a Constant Body Temperature*, Chap. XXVIII.)

There is little question that sympathectomy produces beneficial effects in Raynaud's disease through elimination of vasomotor influence over peripheral vessels. As a result, the digital arteries now are less responsive to local vasoconstricting stimuli and hence the degree and number of episodes of color change are reduced. Furthermore, the application of noxious agents to other parts of the body, which normally causes reflex vasoconstriction, is no longer effective. At the same time, sympathectomy abolishes the aching and stinging pain associated with vasoconstriction. Therefore, in the individual who suffers from numerous severe disabling attacks of digital spasm in one or two extremities, this operation may help control the disorder.

However, the limitations of sympathectomy when utilized in Raynaud's disease must also be considered in the full evaluation of this measure. First, it is well to remember that even after the operation the local application of cold to the digits will still elicit a definite although reduced type of response. Second, there is always the chance that the peripheral arteries will become abnormally sensitive to circulating vasopressor substances, which state might be conducive to an actual increase in the degree and frequency of the episodes of color changes. Such a possibility is enhanced by the fact that dorsal sympathectomy, the operation usually performed in Raynaud's disease, is much more prone to this complication than is lumbar sympathectomy. Finally, one must consider the problem of regeneration of sympathetic nerves, a not uncommon finding after dorsal sympathectomy. (For evaluation of the operation see *Sympathectomy*, Chap. XXVII.)

Summary. The treatment of the patient with Raynaud's disease who does not demonstrate nutritional disturbances consists for the most part of protection of the trunk and extremities from cold and trauma. The vasodilator and sympathetic blocking agents may also be useful in controlling or minimizing the attack. Abstinence from smoking should be enforced if at all possible, while psychotherapy may be indicated in some cases. In all patients reassurance and a simple explanation of the condition and the prognosis are essential parts of the therapeutic program. Sympathectomy plays a definite but limited role in this stage of the condition.

TREATMENT OF THE PATIENT WITH AN ULCERATIVE OR GANGRENOUS LESION

In the case of the patient with Raynaud's disease who develops infected ulcerations or superficial gangrene of the tips of the digits, the treatment is more involved. This consists not only of all the precautions and procedures already enumerated but also steps directed toward the healing of the lesions. In this regard, abstinence from smoking is even more important than in the case of the patient without trophic changes. Medical means should be utilized before resorting to surgical procedures.

Medical Therapy

General Supportive Measures The patient with an ulcer or superficial gangrene should remain indoors as much as possible, use her hands only when absolutely necessary and keep them out of water A well balanced diet is a worthwhile adjunct to treatment Psychotherapy, in the form of reassurance and encouragement is particularly important, since in this stage there is a tendency for the patient to become despondent

Local and Systemic Treatment of Lesions In the presence of secondary infection of the ulceration or superficial gangrene, immediate steps should be taken to eliminate this factor, for otherwise healing will not occur Of value is the determination of the sensitivity of the responsible organisms to available antibacterial agents and the use of the proper drugs for topical and parenteral administration Strict aseptic technic should always be followed when the lesion is cleaned Any necrotic tissue eschars, or loose nails should be removed However, as mentioned before, superficial ulcers associated with Raynaud s disease are frequently very painful, and often the patient will not even allow the lesions to be touched by the physician In fact, she generally prefers to apply the dressings herself Hence when the involved area has to be debrided it may be necessary to resort to a general anesthetic

Surgical Therapy

Sympathectomy If an intensive medical program produces no definite signs of improvement or if the process continues to spread then sympathectomy should be seriously considered At times this procedure will produce spectacular healing of chronic ulcers that were resistant to other therapy (Fig 10) However there is no certainty that sympathectomy will invariably cause healing or that once this has taken place there will not be recurrence of nutritional disturbances or even the appearance of new ones elsewhere on the denervated digits

Summary In the treatment of ulceration or superficial gangrene of Raynaud s disease attempts should be made to reduce the number of attacks of digital color change to a minimum at the same time that the lesions are treated locally and systemically In the latter regard the use of appropriate antibacterial agents may play an important role in the healing of the infected ulcers As adjuncts the various vasodilator and sympathetic blocking agents should be used and abstinence from smoking enforced Only after an adequate period of medical therapy fails to produce improvement or healing of the trophic disturbances should sympathectomy be done

Prognosis

Raynaud s disease is a relatively benign disorder Although it may cause great inconvenience to some patients and even interfere with their daily activity generally it can be controlled to some extent by eliminating the agents initiating the attacks In this regard, it is far less serious than the occlusive arterial vascular disorders in which progression of the pathologic state may occur regardless of

what measures are instituted Even when the relatively rare ulceration or superficial gangrene is present it is usually limited to the distal portions of the digits and hence can be treated by medical or surgical means without the necessity of sacrificing an extremity As a result the life of the patient is never in jeopardy It is of interest that the individuals whose attacks can be precipitated only by cold or in whom functional factors are not particularly prominent are more likely to be free of significant tissue destruction than are those in whom emotional stress is a causative agent[6]

In general it can be stated that in Raynaud s disease there is some advancement of the disorder with the passage of the years in the sense that more digits are involved until a stationary phase is reached Thereafter the condition remains unchanged the patient usually having made a mental and physical adjustment to it

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18 RAYNAUD A G M *D l asphyxie locale et de la gangrène symétrique des extrémités* Paris Rignoux 1862

19 SIMPSON S L BROWN G E and ADSON A W Raynaud s disease Evidence that it is a type of vasomotor neurosis *Arch Neurol & Psychiat* 26 687 1931

CHAPTER

IX VASCULAR ENTITIES PRIMARILY AFFECTING THE ARTERIAL TREE

(*Continued*)

2 CHRONIC OCCLUSIVE ARTERIAL VASCULAR DISORDERS

The two most prevalent and important chronic occlusive arterial vascular disorders thromboangiitis obliterans and arteriosclerosis obliterans possess a number of clinical manifestations in common, with the result that frequently one is misdiagnosed for the other By discussing both in the same chapter, it was felt that greater emphasis could be placed on those characteristics which are of value in differential diagnosis

THROMBOANGIITIS OBLITERANS (BUERGER S DISEASE)

General Considerations

Sex, Age, and Racial Susceptibility

Thromboangiitis obliterans is a chronic recurrent segmental type of phlebitis and arteritis that is characterized by remissions and exacerbations From the time it first became a recognized clinical entity [3] it has held an almost unique position among peripheral vascular disorders because of its unusual clinical features Originally it was considered to be confined exclusively to young males between the ages of 16 and 40 years Although a number of authenticated cases have been reported in females such a diagnosis should still be questioned unless the findings are unequivocal Up to recently it was thought the disease affected only Jews of Slavic extraction but the results of current investigations do not confirm this impression For example a study of patients with thromboangiitis obliterans in a vascular center set up by the Army during World War II revealed that Jews made up 8 3 per cent of the series [1] a figure that is only slightly larger than the proportion of this group in the Armed Forces (approximately 4 per cent) It is of interest that the condition is rarely observed among Negroes

Etiologic Factors

The cause of thromboangiitis obliterans has not been established At one time it was felt that the ingestion of bread made from grain containing ergot was an etiologic factor but this has not been supported by clear-cut evidence Later, dermatophytosis and typhus fever and other infectious diseases were likewise implicated but these views too have failed to receive confirmation Tobacco smoking has always been considered to be linked with the disorder and in fact it is the conviction of some workers that this is the main if not the only etiologic factor [14] Opposed to the latter view however is the fact that although at present smoking is as common among women as among men thromboangiitis obliterans is only infrequently noted in females To explain this disparity it is necessary to assume that the two sexes respond differently to the same stimulus and that this reaction is in some way related to variations in secretion of sex hormones Thus far little evidence has been forthcoming to support such a belief

Systemic Character of the Disease

Although thromboangiitis obliterans is known primarily as a disorder of the blood vessels of the extremities on occasion its effects are widespread Necropsy reports have shown pathologic alterations in the arteries of the heart abdominal organs and brain As a rule the appearance of clinical manifestations indicating involvement in other sites is preceded by the onset of difficulties in the extremities In the case of cerebral lesions there may be transient or permanent hemiplegia aphasia disorientation or loss of memory all of which may clear up in a short time It is possible that the transient nature of the symptoms is due to rapid development of an adequate collateral circulation after thrombosis Obviously when essential organs are affected the changes in the extremities assume a minor role in the clinical picture

Pathology

The pathologic process in thromboangiitis obliterans is generally noted first in the superficial veins of the extremities and later in the main arteries although on occasion this order is reversed Associated with the changes in the vessels themselves is involvement of the surrounding tissues taking the form of a periphlebitis and a periarteritis

In the acute stage microscopic examination reveals a normal media and a lumen filled with a grayish or yellowish mass that can be differentiated from the wall This thrombus consists of either a blood clot in a state of organization or proliferating intimal tissue Foci of polymorphonuclear leukocytes are noted together with characteristic giant cells which resemble the [illegible] y giant cell The [illegible] st be pointed out

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on the opposite side The tests for arterial insufficiency are of little help since most of them will demonstrate a normal response

It would seem then that the diagnosis of the disorder in the incipient stage has to be made almost exclusively on symptoms The history of one or more attacks of superficial migratory thrombophlebitis strongly supports such a possibility Despite the paucity of findings it is the safer course under these circumstances to consider the patient a potential case of thromboangiitis obliterans and treat him accordingly rather than to wait until the vascular changes are more apparent and at the same time irreversible

In the third and somewhat more advanced stage there are generally several definite symptoms and signs of arterial insufficiency Whereas the cramping pain in the calf muscles or in the arch of the foot had first been experienced after walking briskly for a mile or two it may now appear after covering only one half mile or less at a slower pace However this causes no incapacitation and the patient is able to carry out all his daily duties except for having to stop and rest occasionally He may observe that his feet are more responsive to a cold environment and that they are much colder than those of other individuals under similar circumstances Sweating may also be increased Abnormal color changes are usually not of sufficient degree at this stage to be noted by the patient unless he has become conscious of the fact that something is wrong with his feet and hence has centered his attention on them However he may have noticed at times clear-cut attacks of Raynaud's phenomenon (p 115) elicited by exposure to cold

Examination frequently reveals significant changes indicating an impairment in circulation in the limbs Among these is a reduction or even absence of pulsations in one or more large arteries accompanied by decreased oscillometric readings particularly in the distal portion of the extremity There may also be some abnormal color changes such as a positive plantar pallor test a slowness in return of color on placing the limbs in dependency and an increasing cyanosis as they remain in this position (Chap II) Low skin temperature readings may be present in the digits At this time therefore a diagnosis of thromboangiitis obliterans should offer little difficulty

The fourth stage is characterized by further progression of the disease causing exaggeration of all the findings previously noted and the appearance of rest pain especially at night due to an ischemic neuritis (Chap I) Intermittent claudication is more marked and may arise after mild exercise as for example walking a block or less The cramping sensation aching fatigue or numbness is generally limited to a single extremity although the opposite one may also be affected by the obliterative process to a lesser extent (For explanation see *Intermittent Claudication* Chap I)

Examination at this time reveals widespread involvement of such large arteries as the popliteal and its branches in the form of markedly reduced or even absent pulsations These changes are accompanied by very low oscillometric readings Invariably there are a positive plantar pallor test rubor of the toes in the horizontal position and cyanosis in dependency The affected hand or foot is colder than the opposite one and removal of vasomotor tonus (Chap IV) produces little rise in skin temperature in the involved digits The subpapillary venous plexus filling

veins are thickened and bound together in a dense mass of connective tissue at times involving the accompanying somatic nerves * Organization of the thrombus has taken place so that it is now converted into fibrous tissue which completely occludes the lumen of the vessel Recanalization may occur through the formation of new vascular channels lined with endothelium These penetrate the fibrous mass and permit circulation of small quantities of blood Calcification of the wall is absent

Clinical Characteristics

Stages of the Disease

Various attempts have been made to place patients with thromboangiitis obliterans into different clinical categories but none has proved entirely acceptable However, since some plan is necessary for the orderly presentation of the following subject matter, a classification into five stages has been adopted which is based on the site and severity of the pathologic process This has been done with the realization that there is some overlapping of arbitrary groups and that the rate of progression of the occlusive process has not been taken into consideration

In the first stage the predominant involvement is thrombosis of superficial veins in the extremities Seen clinically in about 40 per cent of cases of thromboangiitis obliterans, this state most often precedes by years the onset of obvious arterial disease Occasionally however, the interval may be as little as several months or the venous and arterial changes may occur almost simultaneously The pathologic process in the veins causes a fleeting occlusion of small portions of vessels which is unassociated with any systemic effects The condition appears to travel from segment to segment of the same and different veins in an unpredictable manner and from one limb to another, at times affecting a number simultaneously Because of these characteristics it has been given the name of superficial migratory thrombophlebitis Clinically this disorder resembles thrombophlebitis migrans (Chap XIII), except that the latter never demonstrates signs of associated arterial disease

In the second group there is early involvement of the arterial tree, the complaints being suggestive rather than diagnostic There may be variants of intermittent claudication such as mild pain in the arch of the foot numbness in the toes or slight aching sensation in the calf muscles all initiated by walking and disappearing almost instantaneously on termination of the exercise † The patient may also become aware of the fact that his feet are somewhat colder and perspire more and that there is a decrease in the rate of growth of the nails

Physical examination may at this time reveal very minor or no abnormalities The various peripheral arteries are generally palpable although there may be a slight reduction in the pulsations in one or more as compared with their mates

* This reaction probably explains why vasospasm may be noted in thromboangiitis obliterans The contraction of the connective tissue most likely irritates and then stimulates the sympathetic components present in mixed peripheral nerves

† For clinical characteristics of intermittent claudication see p 4 for pathogenesis see p 4>5

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time and the reactive hyperemia test (Chap II) will generally show significantly delayed responses Despite a marked impairment in arterial circulation, however, there are no obvious signs of loss of viability of the skin

The fifth or final stage of the disease is characterized by such a degree of arterial insufficiency that portions of the tissues are no longer receiving an adequate blood

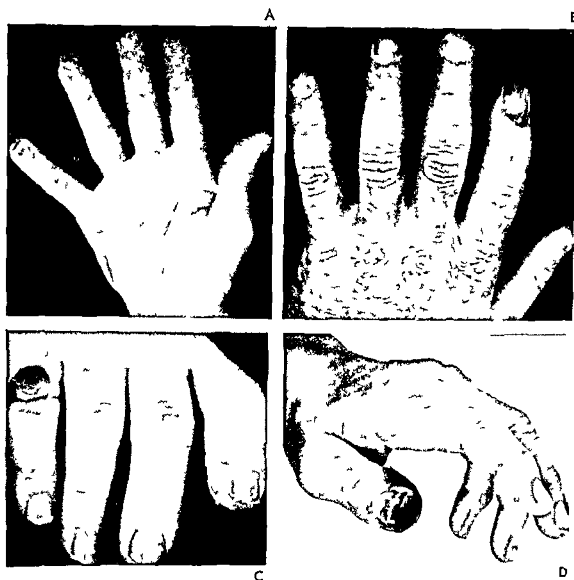


Fig 11 Nutritional disturbances in thromboangiitis obliterans A B, and C Superficial ulceration of fingertips D Superficial gangrene of thumb

supply even at rest Aside from severe intermittent claudication the patient now complains of excruciating pain in the digits with impending or existing nutritional disturbances This symptom is continuous but it may be made more intense by physical activity The patient is apprehensive emotionally upset, and in a poor state of general health because of the interference with his sleep resulting from the persistent pain

A

Rajendr p 51





Fig 1 Nutritional disturbances in thromboangiitis obliterans A and B Gangrene limited to toes C Spread of process onto adjoining portion of foot denoting a much graver prognosis

Examination reveals little that is different from the preceding stage except for changes resulting from a markedly reduced blood supply to the skin and subcutaneous tissue The oscillometric readings are generally very low even at high levels on the extremity In the case of an impending nutritional disturbance there may be a persistent cyanosis or rubor in the affected area which is not altered by changes in position or by digital pressure Despite the fact that there is no break in the skin the presence of these permanent color changes associated with severe pain locally, is fairly conclusive evidence that ulceration or gangrene will occur in

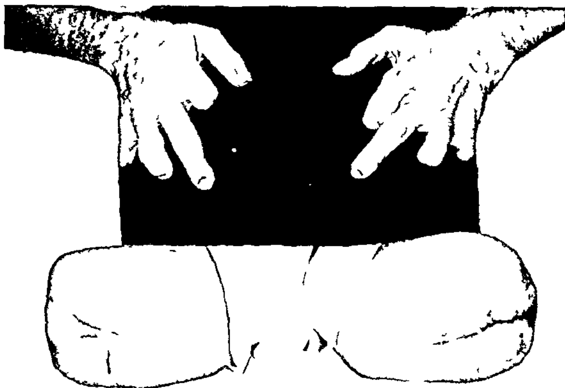


FIG 15 Widespread and severe degree of thromboangiitis obliterans involving all four extremities and necessitating amputation of both lower limbs and several fingers in each hand

the near future The more severe case will already demonstrate such alterations (Figs 11–13) (For discussion of wet or dry gangrene see *Gangrene* Chap VII)

COMPLICATIONS

Complications of thromboangiitis obliterans are infrequent The most serious one is sudden, complete occlusion of a main artery by a thrombus (Chap X) If the process takes place before a sufficiently adequate collateral circulation has developed nutritional disturbances may appear Pulmonary embolism is rare despite the relatively frequent occurrence of superficial thrombophlebitis Acute deep thrombophlebitis is also most unusual[9]

ARTERIOSCLEROSIS OBLITERANS WITH OR WITHOUT DIABETES MELLITUS

General Considerations

Incidence, Age and Sex

From the point of view of incidence arteriosclerosis obliterans is by far the most important of the occlusive arterial vascular diseases With the progressive lengthening of the life expectancy of the diabetic patient through the use of insulin and diet it can be anticipated that the number of cases demonstrating arteriosclerotic changes in the extremities will increase even more in the future This disorder occurs predominantly in patients between the ages of 45 and 70 years however it may also be seen in the third and fourth decades of life and even earlier particularly if associated with diabetes mellitus There is no evidence to indicate that any one group of individuals is affected to a much greater extent than others Nor is there any striking sex predisposition although the condition is present more frequently in males than in females Whereas a history of tobacco smoking is invariably obtained from the patient with thromboangiitis obliterans in arteriosclerosis obliterans this habit may or may not be present

Etiology

A number of views have been advanced regarding the cause of arteriosclerosis obliterans but none has received general acceptance It is the belief of some workers that the pathologic changes are associated with or caused by an error in the metabolism of fat and other lipids [5] In support of this concept a great amount of experimental work has been presented indicating that lesions similar to the atheromatous plaques in human beings can readily be produced in rabbits chickens rats and dogs through the use of a diet rich in cholesterol and animal fat However how much bearing such results have upon the pathogenesis of vascular disease in man is not clear All that can be stated at present is that there is a general association but not an obvious causal relationship between the levels of serum lipids and the incidence of atherosclerosis It is of interest nevertheless that the diabetic patient in whom there is some alteration in fatty metabolism demonstrates the presence of arteriosclerosis at a somewhat earlier age and more commonly than other individuals

Aside from the possible role of blood lipids abnormal vascularization of the arterial wall may also be a significant factor in the development of atheromatous lesions [7, 17] Normally nutrition to an artery is derived from two sources the blood flowing in the vasa vasorum which system ramifies through the outer coats but does not penetrate the intima and the blood in the lumen of the vessel supplying nourishment to the intima In the diseased artery capillaries form which penetrate the intima and anastomose with small twigs arising from the vasa vasorum If subjected to pressure or if the supporting tissue dies these vessels may rupture and cause a small subintimal hemorrhage which in turn will increase the size of the

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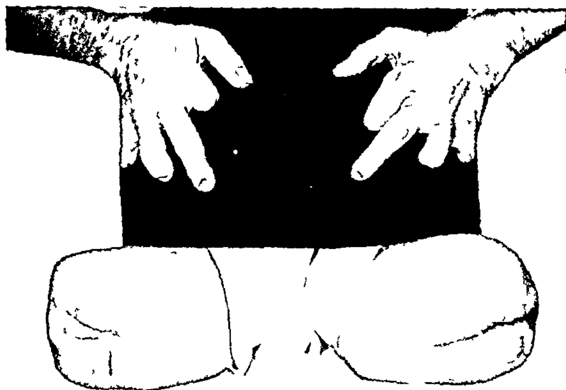


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extent of the occlusive process This is probably because only rarely does the patient in an early stage of the disease seek medical advice for complaints referable to the extremities Evidently the initial rate of occlusion is so slow that as a reduction in the size of the lumen of the main arteries occurs this is balanced by a corresponding increase in the ramification and efficiency of new collateral channels As a result the tissues do not suffer from anoxia

Symptoms

Only when the pathologic process is accelerated while the collateral circulation fails to keep pace will the patient begin to complain of pain in the extremities typical of intermittent claudication The symptom is no different from that observed in thromboangiitis obliterans since the basis is the same namely a discrepancy between the increased metabolic needs of the exercising muscles and the amount of nutrition brought to them through partially occluded vessels incapable of dilating further * Besides the difficulty in walking the patient may also complain of the fairly common symptom of rest pain particularly at night characterized by hyperesthesia tingling and lancinating sensations The basis is probably an ischemic neuritis related to the local chronic state of anoxia

With further progression of the disorder and the appearance of nutritional disturbances severe continuous pain is experienced locally due to actual destruction of tissues At times however with the full development of gangrene and subsequent mummification the symptoms become less or may even disappear In general it can be stated that the pain associated with nutritional disturbances in the patient with arteriosclerosis obliterans is less than in the individual with thromboangiitis obliterans who has a similar sized lesion

Signs

The patient with arteriosclerosis obliterans experiencing difficulties usually demonstrates reduced or absent pulsations in the main arteries of one or both lower extremities and low oscillometric readings at various levels Signs of impaired arterial blood flow are particularly marked in the feet Only infrequently are the vessels in the upper extremities involved and rarely to the point of producing complaints † Associated with the changes in the main channels are such findings as a positive plantar pallor test a delay in the venous filling time and in the return of color in the feet and the appearance of intense cyanosis when the limbs are maintained in dependency (Chap II) The involved foot or feet may be dry and cooler than normal As in the case of thromboangiitis obliterans attacks of Raynaud s phenomenon may appear in the digits on exposure to cold

With progression of the pathologic process eventually the impairment of local circulation becomes so great that the metabolic needs of the tissues are not

For a discussion of the various sta es in which intermittent claudication exists and of symptoms which mimic it see Chap I

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atheromatous plaque Occasionally the lesion may become large enough to produce complete occlusion of the lumen

Another view that has been offered as a possible explanation for the production of atherosclerosis is that this state results from prolonged stress and strain to which arteries are subjected during the life of the individual, and hence that it is a part of the natural aging process Such a belief appears to be supported by the observation that the patient with hypertension develops arteriosclerosis more readily than the normotensive individual Furthermore the portions of the vascular tree which are exposed to the greatest load are frequently those that show the earliest pathologic changes The finding that arteriosclerosis is common in the lower extremities and rare in the upper has also been advanced to support this view, but there is little evidence to indicate that the vascular trees in the two sites are subjected to any significant difference in stress and strain

Systemic Character of the Disease

Arteriosclerosis is a generalized process which affects the brain and heart much more frequently than the extremities However at times the changes may be limited to the extremities alone and hence the absence of the pathologic process elsewhere should not eliminate this entity from the differential diagnosis of an obliterative vascular disorder

Pathology

The typical pathologic changes seen in arteriosclerosis obliterans are degenerative as contrasted with thromboangiitis obliterans which is characterized by an acute inflammatory disturbance The coexistence of diabetes mellitus does not affect the pathologic process The most significant alteration in the wall of the vessel is the atheromatous plaque in the subintimal tissue with thickening of the intima This lesion has the appearance of a raised yellowish mass extending beyond the endothelial surface into the lumen Histologically it is composed of proliferating endothelial cells fibroblasts foam cells and large quantities of lipid material Later calcium deposition may occur The distortion of the intima which follows the process favors thrombi formation When the latter occurs the clot goes through the various stages of organization eventually to produce complete occlusion of the lumen More rapid arterial thrombosis may follow sudden hemorrhage a predisposition which exists in atherosclerosis As in the case of thromboangiitis obliterans, recanalization of the proliferating mass may take place

Associated with the alterations in the intima are degenerative changes in the media These consist of atrophy and necrosis of muscle fibers and replacement by collagenous fibers and subsequently by calcium deposits In only a small percentage of cases do the latter produce the ring like arrangement of Monckeberg s sclerosis Characteristically this type of change is found in the muscular arteries frequently unassociated with atheromatous formation in the intima

Clinical Characteristics

In contrast to thromboangiitis obliterans it is difficult to place individuals with arteriosclerosis obliterans into categories on the basis of severity of symptoms or of

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satisfied even at rest Under such circumstances, slight trauma to the skin may be sufficient to initiate an ulcerative lesion or even gangrene (Fig 14A)

Role of Diabetes Mellitus

The question arises as to whether diabetes mellitus has any influence on the natural course of arteriosclerosis obliterans There are some workers who believe that it has,[11 13 16] while others hold a contrary view[10 1 18] Of interest in this regard is the finding that in the diabetic patient with arteriosclerosis obliterans



Fig 14 Nutritional disturbances in arteriosclerosis obliterans A Superficial gangrene at base of left great toe Skin of rest of foot atrophic and scaly B Extensive gangrene of left foot and leg precipitated by exposure to a moderately low environmental temperature Gangrenous patch also present on right foot

the femoral and popliteal arteries are generally relatively unaffected while the brunt of the pathologic process falls on the smaller more distal vessels

In contrast in the uncomplicated case of arteriosclerosis obliterans the larger arteries are usually also involved in the occlusive process Furthermore there appears to be little doubt that in the presence of diabetes arteriosclerotic disease of the lower extremities is associated with the early occurrence of gangrene while in the nondiabetic individual intermittent claudication commonly precedes this event by years[13]

Another distinguishing point is the fact that if there is a coexisting diabetes the nutritional disturbance has a greater tendency to develop secondary infection with the result that the involved site becomes moist while mummification is delayed

The inflammatory process is generally noted at the junction of necrotic and living tissues and it may spread rapidly through the lymphatics and along tendon sheaths or tissue planes to involve a considerable portion of the extremity (Fig 15B) If it is unchecked marked systemic reactions may occur which place the patient s life in jeopardy It is possible that such changes represent the contribution of diabetes to the undermining of the natural defenses of the body

Complications

There are several serious complications of arteriosclerosis obliterans among which are complete arterial thrombosis (Chap X) and spontaneous arterial aneurysm * Both cause further aggravation of an already existing precarious local blood supply and hence contribute to a graver prognosis



Fig 15 Nutritional disturbances in arteriosclerosis obliterans associated with diabetes A Gangrene of toes and back of heel B Extensive spread of inflammation necessitating wide surgical dissection

Spontaneous Arterial Aneurysm

The aneurysm associated with arteriosclerosis obliterans is generally representative of the true type in the sense that at least one of the coats of the affected segment of vessel is still intact (p 491) The lesion occurs much more frequently in the popliteal artery than in any other vessel in the limbs while involvement of the femoral artery in its course through Scarpa s triangle is next in frequency The predominance of the condition in these sites may be related to the fact that here the vessels are more poorly protected by muscle than in the rest of the lower extremity and are also subjected to repeated trauma in the course of knee and hip movements

Clinical Characteristics The changes associated with spontaneous arterial aneurysm are similar to those noted in the traumatic type (Chap XVII) Local

* Syphilis also plays a role in the etiology of spontaneous aneurysm but this type of lesion occurs usually in patients under the age of 50 years

satisfied even at rest Under such circumstances *slight trauma to the skin* may be sufficient to initiate an ulcerative lesion or even gangrene (Fig 14A)

Role of Diabetes Mellitus

The question arises as to whether diabetes mellitus has any influence on the natural course of arteriosclerosis obliterans There are some workers who believe that it has[11 13 16] while others hold a contrary view[10 1 18] Of interest in this regard is the finding that in the diabetic patient with arteriosclerosis obliterans

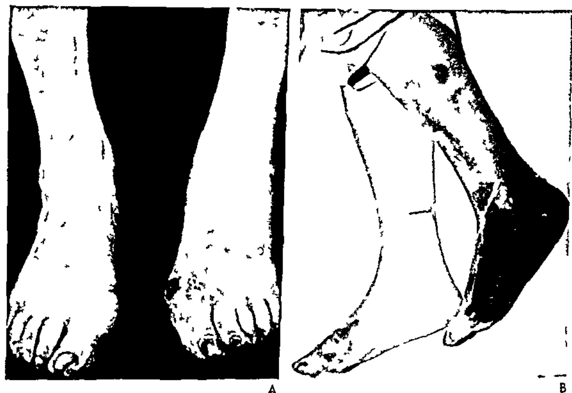


FIG 14 Nutritional disturbances in arteriosclerosis obliterans A Superficial gangrene at base of left great toe Skin of rest of foot atrophic and scaly B Extensive gangrene of left foot and leg precipitated by exposure to a moderately low environmental temperature Gangrenous patch also present on right foot

the femoral and popliteal arteries are generally relatively unaffected while the brunt of the pathologic process falls on the smaller more distal vessels

In contrast in the uncomplicated case of arteriosclerosis obliterans the larger arteries are usually also involved in the occlusive process Furthermore there appears to be little doubt that in the presence of diabetes arteriosclerotic disease of the lower extremities is associated with the early occurrence of gangrene while in the nondiabetic individual intermittent claudication commonly precedes this event by years[13]

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DIFFERENTIAL DIAGNOSIS OF CHRONIC OCCLUSIVE ARTERIAL VASCULAR DISORDERS

Thromboangiitis Obliterans and Arteriosclerosis Obliterans

Considerable difficulty may be encountered in determining whether a patient with a chronic occlusive arterial vascular disorder is suffering from thromboangiitis obliterans or arteriosclerosis obliterans (Table 13) The following points may be found of value in making the differentiation

Of importance is the age of the patient at the time of onset of the condition Thromboangiitis obliterans usually begins in relatively young people 16 to 40 years of age while arteriosclerosis obliterans has its inception in a much older group 45 to 70 years However arteriosclerosis obliterans may occur prematurely in the presence of diabetes Similarly the factor of age is of no diagnostic value if the occlusive arterial disease is first observed when the patient is in his early forties

The coexistence of generalized arteriosclerosis is also helpful in the differential diagnosis For example signs of coronary insufficiency arteriosclerotic changes in the retinal vessels associated with hypertension and thickened and tortuous superficial temporal arteries give support to the view that the changes in the lower extremities are of a similar nature A high blood cholesterol is likewise of use in this regard

There are several other points which are of diagnostic importance Among these is a history of total abstinence from tobacco smoking which would tend to negate a diagnosis of thromboangiitis obliterans on the other hand the presence of superficial migratory thrombophlebitis and pathologic alterations in the blood vessels of the upper extremity would favor such a possibility The x ray findings of calcification of arteries in the extremities can also be given significance since such a change is never noted in uncomplicated thromboangiitis obliterans while being seen on occasion in arteriosclerosis *obliterans* The fact that thromboangiitis obliterans is rarely observed in Negroes and in patients with diabetes must also be taken into consideration in the *differential* diagnosis

Another aid which may be of diagnostic value is arteriography (Chap XXV) In arter [illegible] ntric filling defects in the [illegible] At times the vessel may [illegible] below the block receiving blood through collateral vessels which bridge the obstructed portion (Fig 164) Marked tortuosity of the involved arteries is a characteristic finding

In thromboangiitis obliterans the arteriogram visualizes the patchy distribution of the disease process The lumen is reduced in size in the initial stage and later may show segments of complete occlusion However above and below the ob[illegible] structed portion it is smooth and does not show the filling defects observed [illegible] arteriosclerosis obliterans Furthermore the vessels are less likely to be tortuous [illegible] Whether or not the degree of collateralization offers a differentiating p[illegible] ficult to state for the literature contains conflicting reports

pain, swelling and an increase in the venous pattern of the limb may result from pressure of the enlarging lesion on the neighboring nerves and veins *Symptoms* and signs of ischemia are not present in the uncomplicated cases, since the aneurysm does not interfere with arterial circulation to the tissues distally The diagnosis of the condition depends primarily upon the presence of a pulsating mass * a thrill and bruit over the aneurysm being rather inconstant findings Arteriography (Chap XXV) is a valuable procedure in confirming the clinical diagnosis

Therapy In contrast with traumatic arterial aneurysm, there is no unanimity regarding the treatment of spontaneous arterial aneurysm Against conservative therapy is the fact that this type of lesion may be followed by serious complications (see below) Restorative measures are generally not attempted because the arteriosclerotic vessel does not lend itself readily to such an approach In the case of a popliteal aneurysm aneurysmectomy, preceded by a sympathectomy has resulted in saving the limb in the great majority of cases [8] The presence of an adequate collateral circulation is a prerequisite for surgical therapy and must be determined preoperatively

Another point which must be taken into consideration if the above approach is contemplated is the high operative mortality associated with spontaneous arterial aneurysm A possible explanation is the fact that patients with this type of lesion generally fall into the fifth and sixth decades of life and hence frequently suffer from arteriosclerotic changes in vital organs

Prognosis The outlook in the untreated case of spontaneous arterial aneurysm depends upon whether or not sequelae of this condition appear Among these is the release of small emboli from the clotted material which lodge in distal vessels at times to produce gangrene if the main blood supply has been obstructed Other complications are spontaneous acute thrombosis of the aneurysm and the adjoining portion of artery which may also lead to nutritional disturbances in the limb and rupture and hemorrhage which place the patient s life in danger Of lesser significance is pressure on associated veins and nerves

The prognosis after surgical intervention will depend upon the type and outcome of the operation performed If ligation of the artery and excision of the aneurysm were found to be the only practical approach to the problem whether or not gangrene occurs will be determined by the extent and efficiency of the existing collateral vessels If a restorative operation is successful there should be no difficulties after surgery On the other hand, secondary thrombosis of the graft carries with it the same or even a graver outlook than ligation since in the process of performing the operation collateral branches arising proximally to the lesion are of necessity destroyed

* In the routine examination of the arteries attention is again called to the necessity of placing the patient on his abdomen and palpating the entire popliteal space Otherwise the existence of a popliteal aneurysm may be completely overlooked since pulsations and oscillometric readings in the leg and foot are frequently normal under these circumstances

DIFFERENTIAL DIAGNOSIS OF CHRONIC OCCLUSIVE ARTERIAL VASCULAR DISORDERS

Thromboangiitis Obliterans and Arteriosclerosis Obliterans

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There are several other points which are of diagnostic importance Among these is a history of total abstinence from tobacco smoking which would tend to negate a diagnosis of thromboangiitis obliterans on the other hand the presence of superficial migratory thrombophlebitis and pathologic alterations in the blood vessels of the upper extremity would favor such a possibility The x ray findings of calcification of arteries in the extremities can also be given significance since such a change is never noted in uncomplicated thromboangiitis [illegible]

[illegible] differential diagnosis

Another aid which may be of diagnostic value is arteriography (Chap XXV) In arteriosclerosis obliterans the arteriogram shows eccentric filling defects in the walls of the arteries and segments of complete occlusion At times the vessel may be seen functioning below the block receiving blood through collateral vessels which bridge the obstructed portion (Fig 16A) Marked tortuosity of the involved arteries is a characteristic finding

In thromboangiitis obliterans the arteriogram visualizes the patchy distribution of the disease process The lumen is reduced in size in the initial stage and later may show segments of complete occlusion However above and below the obstructed portion it is smooth and does not show the filling defects observed in arteriosclerosis obliterans Furthermore the vessels are less likely to be tortuous Whether or not the degree of collateralization offers a differentiating point is difficult to state for the literature contains conflicting reports

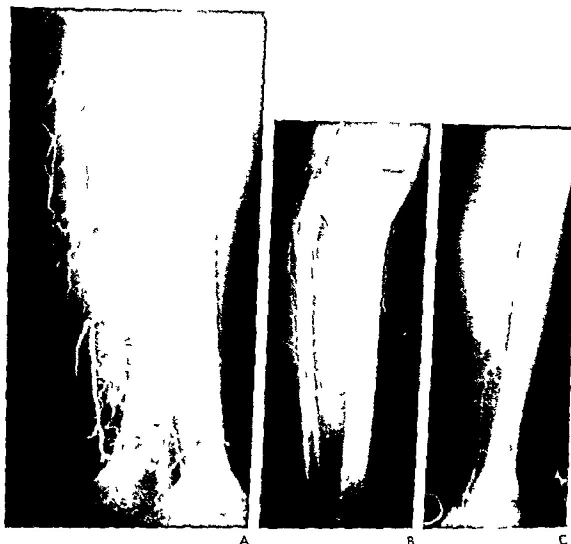


Fig 16 Arteriography in arteriosclerosis obliterans A Segmental block in femoral artery with extensive bridging collaterals and filling of artery below Another block noted at a lower level B Obstruction of popliteal artery with collateral vessels below C Complete obstruction of main arteries of leg with nutrition of limb dependent entirely upon collateral circulation

Monckeberg's Sclerosis

A popular misconception among physicians is the significance attributed to deposition of calcium in the media of large arteries as observed by roentgenography Unfortunately frequently little attempt is made to differentiate this type of benign arteriosclerosis designated as Monckeberg's sclerosis from atherosclerosis the pathologic change in arteriosclerosis obliterans Monckeberg's sclerosis affects the arteries in the lower extremities of young or middle aged persons and produces no symptoms in the limbs Usually the calcific changes are discovered by accident when an x ray is taken for some other reason * Because calcification of

* It is questionable whether a patient with Monckeberg's sclerosis should be informed of this fact for if he is he may develop a marked preoccupation with the circulation to his extremities and thus magnify minor complaints into what he believes are difficulties of major consequence If he is already aware of the situation all efforts should be made to impress him with the innocuous character of the disorder

the media causes some decrease in the distensibility of the blood vessel there results some reduction in pulsations in the main arteries and in the oscillometric readings However the pathologic change does not interfere with the movement of blood and hence there is no impairment in local circulation This is in contrast with the abnormalities seen in arteriosclerosis obliterans It is true that in some patients with the latter disorder calcification of the media may be noted which as has already been mentioned is of value in the differentiation from thrombo angiitis obliterans However, this is merely an associated change and does not have any significance with regard to the degree of existing arterial insufficiency

RAYNAUD S DISEASE

As indicated elsewhere a triphasic color change in the digits elicited by exposure to cold may be part of the clinical picture of both thromboangiitis obliterans and arteriosclerosis obliterans as well as the predominant finding in true Raynaud s disease For this reason the latter entity must be considered in the differential diagnosis of chronic occlusive arterial vascular disorders Of primary importance is the fact that in arteriosclerosis obliterans and thromboangiitis obliterans there are always definite and permanent signs of arterial impairment while in Raynaud s disease the circulation is normal in between attacks The difference in sex inci dence and the age of the patient at the onset of the condition are also significant differential points (Table 13) It is of interest that in Raynaud s syndrome as sociated with thromboangiitis obliterans the color change is generally limited to one or two digits whereas in Raynaud s disease the response is much more wide spread

INFECTIOUS PROCESSES

With the appearance of nutritional changes in chronic occlusive arterial vascular disorders the associated signs of inflammation in the foot or hand may at times be mistaken for an uncomplicated infectious process and treated as such with hot packs or even surgery Since one can expect deleterious effects f [illegible]
tures [illegible]
initia [illegible]
warm [illegible] local blood flow and there are no signs of arterial insufficiency On the other hand in the presence of an occlusive arterial vascular disorder of a degree sufficient to produce this clinical picture the affected site is if anything colder than the other parts of the limb and there are many obvious indications of a markedly reduced arterial circulation

SPECIFIC THERAPY IN CHRONIC OCCLUSIVE ARTERIAL VASCULAR DISORDERS

It [illegible]
mi [illegible]
ro [illegible] obliterans or for arterioscle [illegible] other procedures used in the treatment of chronic occlusive arterial vascular disorders are presented in detail in Chapter XII

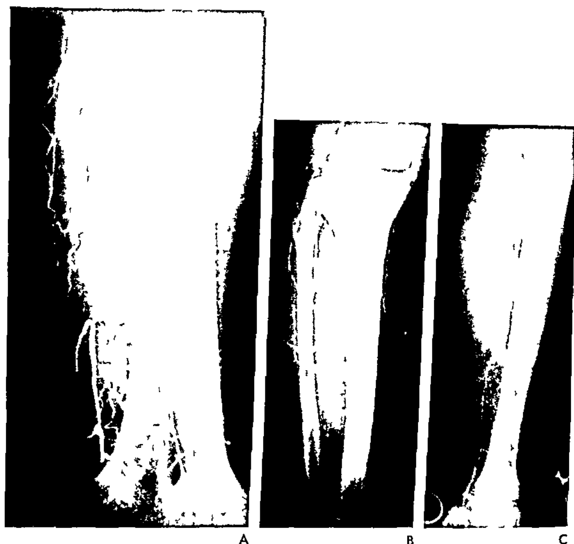


Fig 16 Arteriography in arteriosclerosis obliterans A Segmental block in femoral artery with extensive bridging collaterals and filling of artery below Another block noted at a lower level B Obstruction of popliteal artery with collateral vessels below C Complete obstruction of main arteries of leg with nutrition of limb dependent entirely upon collateral circulation

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Table 13 (continued)

	Raynaud s disease	*Thromboangiitis obliterans*	*Arteriosclerosis obliterans*
Pulsations in main arteries & oscillometric readings	Normal	Pulsations in some of the main arteries always reduced or ab sent oscillometric readings absent or reduced	Pulsations in some of the main arteries always reduced or ab sent oscillometric readings always reduced or absent
Signs of vasospasm	May be present between episodes of color changes	May be present	Usually not present
Permanent color changes	Possibly a slight cyanosis	Cyanotic rubor may be present	Cyanotic rubor may be present
Onset and extent of gangrene and ulceration	Late complication infrequently present & of a minor degree limited to tips of digits rarely is amputation of a digit necessary	Usually a slow process but may be quite extensive necessitating amputation of a limb in many instances	May occur suddenly and may be quite extensive necessitating amputation of a limb in many instances
Infection & pain associated with gangrene and ulceration	Infection may be present with ulceration pain may be very severe	Infection rarely present Pain may be very severe	Infection frequently present if diabetes coexists less frequently present in the senile type pain generally not too severe
Other nutritional changes	Sclerodactylia thickening of skin of finger tips loss of subcutaneous tissue	Generally not present	Loss of normal consistency of skin producing parchment-like appearance
Generalized arteriosclerosis	Usually not present	Usually not present	May be present
Arteriography	No abnormalities unless spasm is produced by injection of material	Uniform decrease in size of lumen with some collateral circulation	Irregular decrease in size of lumen with multiple filling defects & extensive collateral circulation
Soft tissue x ray technic	No signs of calcification of media	No signs of calcification of media	Calcification of media (Monckeberg's sclerosis) may or may not be present

Table 13 Differential Diagnosis of Thromboangiitis Obliterans Arteriosclerosis Obliterans, and Raynaud's Disease

	Raynaud's disease	*Thromboangiitis obliterans*	*Arteriosclerosis obliterans*
Age at time of onset	20-45 years	16-40 years	45-70 years at a much earlier age if associated with diabetes
Sex	Predominantly in females	Almost invariably in males	Affects both sexes slight preponderance of males
History of tobacco smoking and effect of habit on progress of disease	Habit may or may not be present no particular effect on progress of disease	Habit invariably present causes definite progress of disease	Habit may or may not be present effect on progress of disease not as apparent as in thromboangiitis obliterans
Pathologic process	No changes observed in vessels in most instances if condition is long standing thickening of media & thrombosis of terminal branches may be present	Inflammatory panarteritis primarily affecting subintima thrombosis may follow both vein & artery involved with some irritation of sympathetic nerve fibers in adjacent peripheral mixed nerve	Degenerative process affecting intima of large arteries producing plaques which extend into lumen secondarily plaques degenerate or erode & thrombosis occurs veins not involved
Vessels and extremities involved	Digital arteries of fingers and toes only fingers involved more often than toes	Medium sized or small arteries ulnar radial post tibial & dorsalis pedis later plantar palmar & digital arteries & then large arteries veins also involved lower extremities affected more often than upper	Primarily the large vessels in the lower extremities iliac femoral & popliteal later dorsalis pedis & posterior tibial rarely the vessels of upper extremities veins not involved
Intermittent claudication	Never present	Almost always present	Almost always present
Increased responsiveness to cold	Generally present	Usually not present	Usually not present
Superficial migratory thrombophlebitis	Absent	Present in about 40% of cases	Absent
Attacks of digital pallor or cyanosis initiated by cold or emotion	Always present diagnosis depends on this finding	May be present in about one third of cases	Present infrequently

Table 15 (continued)

	Raynaud s disease	*Thromboangiitis obliterans*	*Arteriosclerosis obliterans*
Pulsations in main arteries & *oscillometric readings*	Normal	Pulsations in *some of* the main arteries always reduced *or* absent oscillometric readings absent or reduced	Pulsations in some of the main arteries always reduced or absent oscillometric readings always reduced or absent
Signs of vasospasm	*May* be present *between* episodes of color changes	May be present	Usually not present
Permanent color changes	Possibly a slight cyanosis	Cyanotic rubor may be present	Cyanotic rubor may be present
Onset and extent of gangrene and *ulceration*	Late complication infrequently present & of a minor degree limited to tips of digits rarely is amputation *of a* digit necessary	Usually a slow process but may be quite extensive necessitating amputation of a limb in *many* instances	May *occur* suddenly and *may* be quite extensive necessitating amputation of a limb in many instances
Infection & pain associated with gangrene and *ulceration*	Infection may be present with ulceration pain may be very *severe*	Infection rarely present Pain may be very severe	Infection *frequently* present if diabetes coexists less frequently present in the senile type pain generally not too severe
Other nutritional changes	Sclerodactylia thickening of skin of finger tips loss of *subcutaneous* tissue	Generally not present	*Loss* of normal consistency of skin producing parchment-like appearance
Generalized arteriosclerosis	Usually not present	Usually *not* present	May be present
Arteriography	No abnormalities unless spasm is *produced* by *injection* of material	Uniform decrease in size of *lumen* with some collateral circulation	Irregular decrease in size of lumen with multiple filling defects & extensive collateral circulation
Soft tissue x ray *technic*	No signs of calcification of *media*	No signs of calcification of *media*	Calcification of media (Monckeberg's sclerosis) may or may not be present

Thromboangiitis Obliterans

In the Absence of Nutritional Changes In the case of the patient with thromboangiitis obliterans whose main complaint is intermittent claudication no definitive therapy is available The various dilator drugs and sympathetic blocking agents are of little value as are also such procedures as intermittent venous occlusion, Pavaex boot oscillating bed postural exercises, and pancreatic extracts The intravenous administration of hypertonic saline solution (3–5%) has been given an extensive clinical trial,[1] but the method appears impracticable for clinical use because a great number of injections are necessary, extending over a period of a year or two Furthermore, the results obtained in various laboratories are by no means consistent or unequivocal

It would seem then that therapy for the patient with no nutritional disturbances is, for the most part of a general nature, consisting primarily of abstinence from smoking and local care of the feet (Chap XII) The treatment of attacks of superficial migratory thrombophlebitis is similar to that outlined for thrombophlebitis migrans (See *Treatment* of thrombophlebitis migrans Chap XIII)

In the Presence of Nutritional Changes In the case of the patient with ulceration or gangrene typhoid vaccine should be utilized if the lesion is found resistant to the medical regimen outlined in Chap XII Such a measure causes a rise in body temperature and a consequent augmentation in cutaneous blood flow, a response which is of value in the healing of an ulcer To produce the desired effect the vaccine is injected intravenously in gradually increasing amounts using one of the standardized commercial products * rather than stock vaccines which have the disadvantage of giving variable results The course of treatment ordinarily utilized consists of the following

A small initial dose of 5 or 10 million bacteria is used to gauge the response of the patient Then through a series of preliminary injections given on alternate days, the amount is determined which will consistently produce a rise in body temperature to about 38 7° C (101° F) This quantity is utilized during the entire period of therapy unless a tolerance develops under which circumstances the dosage is increased Conversely if the response becomes more marked than desirable the strength of the injection is decreased

The peripheral vascular alterations produced by typhoid vaccine are generally quite consistent Approximately two to three hours after the intravenous administration of the material the patient begins to develop a chilly sensation or an actual shaking chill This is associated with an intense vasoconstriction of cutaneous vessels producing a cold pale or blue skin and a rise in body temperature There then follow a generalized vasodilatation of cutaneous vessels and profuse sweating both of which result in an acceleration in the rate of heat loss These responses begin during the period of elevated body temperature and continue for several hours afterward During this time the skin is pink and warm

No attempt should be made to evaluate the measure until at least 10 injections have been given on alternate days If in the period of time required for this no

* *B typhosus* 50 million *B para* A 25 million and *B para* B 25 million made up to 1 cc

signs of improvement are noted then it can be assumed that probably little benefit would result from further treatment On the other hand if there is any indication of healing at the margins of the ulcer if a definite line of demarcation appears in the gangrenous site or if the associated pain is reduced it is worthwhile continuing the therapy for a longer interval

Untoward responses to the administration of typhoid vaccine include chills headache nausea vomiting and malaise frequently of a degree to make the patient uncomfortable However most individuals are willing to undergo the unpleasant experience repeatedly provided some improvement in their condition is noted It is necessary to have routine microscopic examinations of the urine during the course of the therapy since on occasion signs of kidney irritation as manifested by the appearance of red blood cells may occur Under such circumstances it is probably advisable to discontinue the procedure Aside from these relatively minor side effects more serious complications have been reported These include thrombosis in uninvolved arteries during the initial period of intense peripheral vasoconstriction and at times marked circulatory disturbances consequent to the rise in temperature

It would seem then that typhoid vaccine should be limited to the young patient with a relatively normal cardiovascular system who shows signs of impending or existing gangrene or ulceration of a toe or toes provided that the process in the skin is not too widespread that infection is not marked and that osteomyelitis does not exist (For use of sympathectomy in treatment of nutritional changes see p 206)

Arteriosclerosis Obliterans

In the Absence of Nutritional Changes The patient with arteriosclerosis obliterans whose main complaint is intermittent claudication should receive a trial course of treatment with one of the pancreatic extracts in an attempt to increase his walking ability Two products are available commercially Depropanex[2, 4, 8] and Padutin Because the results are somewhat better with Depropanex and because it is more simply administered the present discussion will be limited to the use of this drug

In many instances the patient can be taught to give the medication himself since it does not elicit any untoward effects The regimen utilized is as follows Two cc are given intramuscularly first three times a week for 3 weeks then twice a week for 3 weeks and finally once a week for 3 weeks It is necessary to keep the solution refrigerated at all times

The response to Depropanex varies In most instances no improvement in walking takes place during the first two or three weeks of treatment thus supporting the impression that if a therapeutic response occurs later this can be attributed to the action of the drug and not to the psychic effects of parenteral administration of any medication If no alteration in walking ability is experienced after 4 or 5 weeks of therapy it is advisable to discontinue the drug since generally further administration is of little value On the other hand if even minimal improvement has occurred in this period then the full course should be given An early beneficial action may take the form of a slight increase in walking ability or

Thromboangiitis Obliterans

In the Absence of Nutritional Changes. In the case of the patient with thromboangiitis obliterans whose main complaint is intermittent claudication no definitive therapy is available. The various dilator drugs and sympathetic blocking agents are of little value, as are also such procedures as intermittent venous occlusion, Pavaex boot, oscillating bed, postural exercises and pancreatic extracts. The intravenous administration of hypertonic saline solution (3–5%) has been given an extensive clinical trial[16] but the method appears impracticable for clinical use because a great number of injections are necessary extending over a period of a year or two. Furthermore, the results obtained in various laboratories are by no means consistent or unequivocal.

It would seem then that therapy for the patient with no nutritional disturbances is, for the most part, of a general nature, consisting primarily of abstinence from smoking and local care of the feet (Chap. XII). The treatment of attacks of superficial migratory thrombophlebitis is similar to that outlined for thrombophlebitis migrans. (See *Treatment* of thrombophlebitis migrans, Chap. XIII.)

In the Presence of Nutritional Changes. In the case of the patient with ulceration or gangrene, typhoid vaccine should be utilized if the lesion is found resistant to the medical regimen outlined in Chap. XII. Such a measure causes a rise in body temperature and a consequent augmentation in cutaneous blood flow, a response which is of value in the healing of an ulcer. To produce the desired effect, the vaccine is injected intravenously in gradually increasing amounts, using one of the standardized commercial products * rather than stock vaccines, which have the disadvantage of giving variable results. The course of treatment ordinarily utilized consists of the following.

A small initial dose of 5 or 10 million bacteria is used to gauge the response of the patient. Then through a series of preliminary injections given on alternate days the amount is determined which will consistently produce a rise in body temperature to about 38.7° C. (101° F.). This quantity is utilized during the entire period of therapy unless a tolerance develops, under which circumstances the dosage is increased. Conversely, if the response becomes more marked than desirable, the strength of the injection is decreased.

The peripheral vascular alterations produced by typhoid vaccine are generally quite consistent. Approximately two to three hours after the intravenous administration of the material the patient begins to develop a chilly sensation or an actual shaking chill. This is associated with an intense vasoconstriction of cutaneous vessels, producing a cold, pale or blue skin, and a rise in body temperature. There then follow a generalized vasodilatation of cutaneous vessels and profuse sweating, both of which result in an acceleration in the rate of heat loss. These responses begin during the period of elevated body temperature and continue for several hours afterward. During this time the skin is pink and warm.

No attempt should be made to evaluate the measure until at least 10 injections have been given on alternate days. If in the period of time required for this no

* *B. typhosus*, 50 million, *B. para. A*, 25 million and *B. para. B*, 5 million made up to 1 cc.

upper extremity necessary although a finger or fingers may have to be treated surgically At times amputation of a limb must be performed not because of extensive gangrene but in order to control pain of a degree sufficient to undermine the stability of the patient's nervous system Usually operative procedures are associated with a low mortality because most of the individuals affected by the disease are young

ARTERIOSCLEROSIS OBLITERANS

In contrast to thromboangiitis obliterans arteriosclerosis obliterans is a generalized degenerative disorder which frequently involves vital organs For the most part therefore the prognosis as to life will be markedly influenced by the severity of coexisting changes in sites other than the extremities

The pathologic process in the limbs is progressive so that the maintenance of viability of tissues will eventually depend almost entirely upon the collateral circulation If the latter continues to grow at a rate which is sufficient to offset the slow occlusion taking place in the main arterial trunks then nutritional disturbances will not appear Under these circumstances provided the feet are not traumatized or exposed to noxious stimuli the patient will be able to lead a fairly normal life except for difficulty on walking a situation which can be controlled to some extent by various therapeutic measures Of great importance in helping the patient make a satisfactory mental and physical adjustment to his handicap is a simple but comprehensive discussion of his condition by the physician with emphasis on the fact that compensatory mechanisms are always at work to counteract the reduced blood flow in the limb

The outlook may be entirely different however if certain factors come into play One of these is an acceleration of the rate of closure of the main vessels [illegible] As a consequence the secondary [illegible] in adequate local circulation and [illegible] of tissues will follow A similar state may be produced by trauma exposure to cold and other noxious stimuli since these agents too are capable of destroying an existing effective balance between rate of occlusive process and growth of new vessels Diabetes contributes to the seriousness of the situation through its deleterious influence on the resistance of tissues to infection The fact that it is necessary to treat most of the resulting nutritional disturbances surgically also affects the prognosis For as a rule patients with arteriosclerosis obliterans are relatively poor operative risks inasmuch as they generally fall into the fifth and sixth decades of life and hence are probably suffering from associated arteriosclerotic changes in vital organs

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a lesser degree of pain experienced on covering the previous claudication distance. After treatment is completed, the patient should be observed for any regression and if this is noted, another course of one or two injections weekly should be given for 8 to 10 weeks. Generally it is necessary to repeat the medication at intervals of approximately six months in order to maintain the improvement in walking.

The best therapeutic effects are usually observed in the patient who originally *had to stop after covering a half block or less* while the one with a pretreatment claudication distance of 2 blocks or more frequently does not show proportionate improvement. In general about 60–70 per cent of the cases can be expected to manifest a therapeutic effect with Depropanex and about 50 per cent with Padutin.[2]

As in the case of thromboangiitis obliterans, a number of other measures have been used in arteriosclerosis obliterans, but for the most part the physiologic and clinical support for their therapeutic value is equivocal. In this category fall vasodilating drugs, sympathectomy and the different mechanical procedures, such as the oscillating bed, Buerger's exercises, intermittent venous occlusion and Pavaex. (For further discussion of some of these procedures, see Chap. XII.)

In the Presence of Nutritional Changes. In the case of the patient who is suffering from ulceration or gangrene no specific therapy is available. Typhoid vaccine is *not indicated since the compensatory cardiovascular mechanisms elicited* by the fever may prove inadequate due to associated changes frequently found in the elderly patient suffering from arteriosclerosis obliterans. Therapy, therefore consists primarily of the local care of the lesion (Chap. XII). *If* diabetes is also present more scrupulous attention to the wound is important because of the resulting increased susceptibility to infection and the tendency for the process to pass through the lymphatics. At the same time, there may be need for a greater quantity of insulin. (For the use of sympathectomy in the treatment of nutritional disturbances, see p. 206.)

PROGNOSIS OF CHRONIC OCCLUSIVE ARTERIAL VASCULAR DISORDERS

Thromboangiitis Obliterans

In general the prognosis as to life is good in thromboangiitis obliterans. This is because similar pathologic changes in vital organs are relatively rare. If present the latter may definitely influence the outlook depending upon the age at which *such alterations* occur, the degree of involvement and the rapidity of the process.

With regard to the maintenance of viability in the involved limbs if the important therapeutic measures of abstinence from smoking and protection of the tissues from trauma and vasoconstricting stimuli are conscientiously carried out, in many instances the patient will enjoy a normal life span without the appearance of nutritional disturbances. *On the other hand failure to obey these rules* will frequently contribute to the production of ulceration and gangrene requiring amputation of digits or of a portion of a limb or limbs. Rarely is removal of an

upper extremity necessary although a finger or fingers may have to be treated surgically. At times amputation of a limb must be performed not because of extensive gangrene but in order to control pain of a degree sufficient to undermine the stability of the patient's nervous system. Usually operative procedures are associated with a low mortality because most of the individuals affected by the disease are young.

ARTERIOSCLEROSIS OBLITERANS

In contrast to thromboangiitis obliterans, arteriosclerosis obliterans is a generalized degenerative disorder which frequently involves vital organs. For the most part, therefore, the prognosis as to life will be markedly influenced by the severity of coexisting changes in sites other than the extremities.

The pathologic process in the limbs is progressive so that the maintenance of viability of tissues will eventually depend almost entirely upon the collateral circulation. If the latter continues to grow at a rate which is sufficient to offset the slow occlusion taking place in the main arterial trunks, then nutritional disturbances will not appear. Under these circumstances, provided the feet are not traumatized or exposed to noxious stimuli, the patient will be able to lead a fairly normal life except for difficulty on walking, a situation which can be controlled to some extent by various therapeutic measures. Of great importance in helping the patient make a satisfactory mental and physical adjustment to his handicap is a simple but comprehensive discussion of his condition by the physician, with emphasis on the fact that compensatory mechanisms are always at work to counteract the reduced blood flow in the limb.

The outlook may be entirely different, however, if certain factors come into play. One of these is an acceleration of the rate of closure of the main vessels due to conditions beyond the control of therapy. As a consequence, the secondary vascular system will be unprepared to supply an adequate local circulation, and hence death of tissues will follow. A similar state may be produced by trauma, exposure to cold and other noxious stimuli, since these agents, too, are capable of destroying an existing effective balance between rate of occlusive process and growth of new vessels. Diabetes contributes to the seriousness of the situation through its deleterious influence on the resistance of tissues to infection. The fact that it is necessary to treat most of the resulting nutritional disturbances surgically also affects the prognosis. For as a rule, patients with arteriosclerosis obliterans are relatively poor operative risks, inasmuch as they generally fall into the fifth and sixth decades of life and hence are probably suffering from associated arteriosclerotic changes in vital organs.

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a lesser degree of pain experienced on covering the previous claudication distance After treatment is completed, the patient should be observed for any regression, and if this is noted, another course of one or two injections weekly should be given for 8 to 10 weeks Generally it is necessary to repeat the medication at intervals of approximately six months in order to maintain the improvement in walking

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CHAPTER

X VASCULAR ENTITIES PRIMARILY AFFECTING THE ARTERIAL TREE

(*Continued*)

3 COMPLETE OCCLUSION OF ARTERIES

Complete obstruction of main arteries in the extremities may be caused by a number of different mechanisms Some are instantaneous in their effect such as intense vasospasm or lodgment of an embolus while others—such as a slowly forming thrombus—persist for a long time before producing complete closure The present chapter deals with those types of arterial occlusion which result from disease states

ARTERIAL EMBOLISM

General Considerations

A peripheral vascular disorder which requires immediate clinical recognition is sudden occlusion of a main artery to an extremity by an embolus More than any other circulatory condition this can be considered a real emergency since the steps taken in the first few hours after its inception may determine whether or not the limb will remain viable Therefore in all cardiac patients but especially in those who are potential candidates for embolus formation it behooves the physician continually to be on the alert for the appearance of those symptoms and signs which are diagnostic of this state

Anatomic Considerations

Sites of Origin of Emboli Arterial emboli may arise from a number of different locations in the cardiovascular system The most frequent is the left atrium (auricle) particularly in the presence of long standing auricular fibrillation due to mitral valvular heart disease arteriosclerotic heart disease hypertension or rarely hyperthyroidism A dilated left atrium even when associated with a regular sinus rhythm may also be the source of thrombus formation The next most common site is the left ventricle (Fig 17A) Gen

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erally the focus is a mural thrombus associated with a myocardial infarct which has extended to the endocardial surface Under such circumstances the embolic episodes may occur a week or two after the onset of the original condition Mural thrombi may likewise form in a large dilated left ventricle

There are several much more infrequent sites of origin of emboli Among these is the cavity of an aneurysm of a main artery in the limb or of the abdominal aorta the separation of a piece of clot in the sac being followed by its liberation into the blood stream Similarly dislodgment of a mural thrombus which has developed upon an arteriosclerotic plaque in the aorta may cause occlusion of a distal branch Occasionally emboli may arise in the veins of the leg enter the right side of the heart and pass through a patent foramen ovale to reach the systemic circulation (paradoxical embolus) In the presence of acute or subacute bacterial endocarditis friable portions of involved valves may break off and form infected emboli Finally pulmonary phlebitis associated with lung infections has also been implicated in the formation of systemic embolization

Sites of Predilection Emboli are seldom large enough to occlude such large arteries as the aorta or common iliacs except at their bifurcation where the lumen is suddenly narrowed and a saddleback anatomic arrangement is present (Fig 17B) and rarely at a site of a pre-existing atherosclerotic ulcer On the other hand the arteries in the extremities are the site of lodgment of approximately two thirds of systemic arterial emboli Again, the location of occlusion is generally at vessel bifurcations although any portion can conceivably be affected provided it manifests a rapid reduction in size of lumen Several branches may be obstructed simultaneously if a soft thrombus breaks on striking a bifurcation of an artery The incidence of lodgment of emboli in the main vessel and those subdivisions which supply the extremities conforms to the following order femoral (above the origin of the deep femoral) popliteal common iliac brachial bifurcation of the aorta subclavian external iliac femoral (below the origin of the deep femoral) posterior tibial radial ulnar and anterior tibial arteries [2]

Pathogenesis

With sudden obstruction of a previously normal main arterial channel in an extremity not only is there immediate cessation of blood flow through the vessel below the level of closure but at the same time there is spasm of the collateral channels in the involved limb which further aggravates the state of anoxia of the distal tissues The mechanism responsible for the latter response is a reflex arc of which the sympathetic fibers are the efferent arm initiated by a focus of irritability in the occluded segment of artery

CLINICAL MANIFESTATIONS

Early Symptoms

Sudden occlusion of a main artery to a limb by an embolus usually causes the immediate onset of pain sharp or dull and generally quite severe On occasion, however it may be absent entirely If the obstruction is in the lower extremity the patient may complain of a dead sensation in the foot and paresthesias in

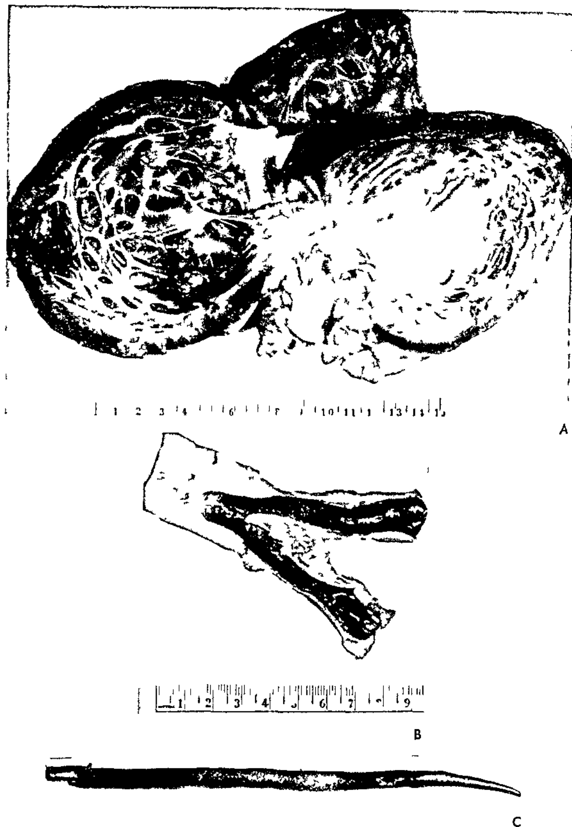


FIG 17 A Mural thrombus in left ventricle (following a myocardial infarction) associated with embolic episodes in the right lower extremity B Embolus at the bifurcation of the left common iliac artery with propagation into the external and internal iliac arteries C Embolus removed from left femoral artery

The impaired cutaneous circulation results in less heat being brought to the surface of the limb and hence in a low skin temperature This is most apparent in the distal portion of the extremity and becomes less prominent as the examining hand moves proximally up the limb Although in most instances the skin temperature of the digits of the opposite normal extremity is higher than those of the involved limb in some patients the difference is not marked This is due to the fact that the vasospasm associated with sudden occlusion of a main artery may also cause

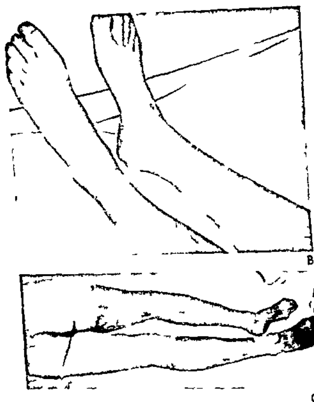


Fig 18 (Continued) B Occlusion of left femoral artery producing irreversible cyanotic mottling of foot and leg C Saddle embolus at bifurcation of aorta causing gangrene of both lower extremities

constriction of the arterial tree of the normal limb and a lowered cutaneous temperature in this site also

Of value in determining the presence of an occlusion of an artery by an embolus are the neurologic findings resulting from ischemia of peripheral nerves Among the most common diagnostic signs is a stocking glove anesthesia or hypesthesia which follows no anatomic nerve distribution and which resembles the type of response noted in patients suffering from hysteria Usually the distal portion of the limb demonstrates anesthesia with the segment above it showing signs of impaired rather than absent sensation There may also be a region of hyperesthesia proximal to the latter Aside from sensory changes impairment in

the toes Frequently he will state that he feels as though he is walking on a block of wood He soon finds that he is unable to move his toes freely or dorsiflex his foot *All* these symptoms are the result of a severe degree of ischemia of all tissues including the peripheral nerves

Besides the distress in the distal portions of the limb, the patient generally also experiences pain at the level of the occlusion This is frequently of a *short* duration and is probably due to spasm of the involved segment of vessel, although *a periarterial inflammatory reaction may also occur, which prolongs the symptoms*



FIG 18 Occlusion of main vessels in lower extremities by emboli A *Occlusion of* left common iliac artery resulting in gangrene of foot and leg

Early Signs

The various physical findings noted in arterial embolism are also the result of marked impairment or complete absence of circulation in the extremity The first sign is an emptying of the subpapillary venous plexus of blood producing a cadaveric pallor of the skin which may be broken by islands of cyanosis due to trapping of blood in certain portions of the cutaneous vessels (Fig 18B) Since there is little arterial inflow the superficial veins are collapsed and barely visible Generally, the affected extremity may appear smaller in circumference than its mate because of the reduced quantity of blood it contains

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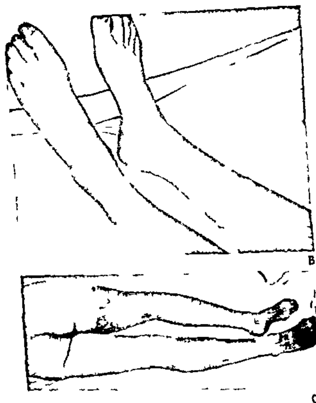


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tion of the acute obstruction although at times the symptoms may first occur in one and after several hours be experienced in the other Such a delay is probably due to the fact that the embolus although present at the bifurcation of the aorta first occludes only one common iliac artery and then as propagation takes place the other is obstructed Similarly the physical findings may be noted in one and later in the other In some instances the lower portion of the abdominal wall may demonstrate mottled irreversible cyanosis due to an associated impairment of its circulation (Table 14)

If the site of obstruction is in one external iliac artery the findings are similar to the above except that the involvement is limited to a single extremity and no changes are noted in the abdominal wall Under these circumstances pulsations should not be felt in the femoral artery below Poupart s ligament although on occasion synchronous movement of this vessel with cardiac systole has been interpreted as such Evidently with each heart beat the column of blood in the common iliac artery sets the embolus into vibration the transmission of which is construed as a pulsation Therefore in every instance in which occlusion of the iliofemoral artery is suspected it is necessary to determine whether or not pulsations are present in the external iliac artery Unless the patient is very obese this can be accomplished by palpation deep in the lower quadrant of the abdomen At the same time the abdominal aorta should be examined *

In the case of involvement of the popliteal artery frequently a periarterial inflammatory reaction is noted producing a tender palpable localized swelling in the popliteal space If the embolus has lodged at the bifurcation of the vessel the symptoms are now located in the calf with the mass being much more indefinite in outline although just as tender The fact that oscillometric readings even though markedly reduced can still be obtained below the knee when an embolus is located at the bifurcation of the popliteal artery is of considerable importance in differentiating this condition from one in which the full length of the vessel is occluded In the latter case all oscillometric readings on the leg are zero

Location of the embolus in either the posterior tibial or dorsalis pedis artery occurs rarely Aside from the loss of pulsation in the involved vessel clinical findings are minimal since the collateral circulation from the other normal vessel is generally sufficient to take care of the metabolic needs of the tissues of the foot

Localizing Signs in the Upper Extremity The axillary or brachial artery is a relatively infrequent site of lodgment of an embolus When complete occlusion occurs pulsations and oscillometric readings disappear at levels on the arm just above the elbow and on the entire forearm while the hand becomes pale and cold with a certain amount of cyanotic mottling in the fingers Ability to perform fine movements may be impaired and there may be a wrist drop Response to pin prick is reduced or absent in the fingers

In the case of a somewhat more common site the bifurcation of the brachial artery the clinical findings are similar to those already described, except that pulsations can be felt in the distal portion of the brachial artery as far as the

* For differential points of an embolus in the iliofemoral artery or at the bifurcation of the femoral artery see Table 14

motor function may be present, consisting of difficulty or inability to move the toes, varying degrees of foot drop and less frequently, comparable changes in the fingers and wrist

The occlusion of a main artery, together with the associated vasospasm, leads to marked changes in arterial pulsations and oscillometric readings Below the level of occlusion both are absent while immediately above this point, the oscillometric readings, at least, may actually be greater than those observed at a comparable site on the opposite normal limb The latter type of change may be a reflection of the backward thrust which occurs when the oncoming column of blood meets the obstruction offered by the trapped embolus, this resulting in a greater distension of the proximal segment of vessel with each cardiac systole *

Determination of Level of Occlusion

General Precautions in Localization On the basis of the physical findings, it is frequently possible to locate the site of arterial occlusion, keeping in mind that the embolus has a predilection for points of bifurcation or narrowing of the vessels Such information is not only essential if embolectomy is contemplated but also of great importance in arriving at a proper prognosis However, before presenting those points which are useful in determining the exact site of occlusion in a specific instance, it is advisable to discuss certain precautions that apply to the problem in general

First it must be pointed out that the transition zone between normal and reduced cutaneous temperature and between normal and reduced sensation is only of value as a gross indication of the level of the occlusion Evidently the existence of a collateral circulation in the proximal portion of the limb contributes to placing the boundary in each case a variable distance below the actual site of embolism On the other hand the level of pallor may be higher than anticipated because of the presence of a superimposed arteriospasm

Second arteriospasm may likewise be responsible in part for reduced or absent pulsations in main vessels as well as similar changes in oscillometric readings Therefore, whenever there is any question the determined site of localization of the lesion should be re evaluated following temporary sympathetic denervation If vasospasm exists to any extent such a step will cause a significant reduction in the severity of the signs thus pointing to a lower level of occlusion Pulsations may even return to main arteries proximally and oscillometric readings may now be obtainable at higher locations on the limb

Localizing Findings in the Lower Extremity In the case of an embolus lodged at the bifurcation of the aorta there may be some prodromal complaints such as abdominal pain with perhaps an accompanying nausea and vomiting A sudden excruciating pain in both lower extremities is usually the initial indica

* Attention must again be called to the necessity of comparing oscillometric readings obtained at various levels on the involved side with comparable sites on the normal side This step is particularly important in the presence of auricular fibrillation since in this condition such measurements may be reduced even in the unaffected limb Hence under these circumstances only the existence of significant differences between the two sides is of any value in the diagnosis of arterial embolism

Table 14 Location of Site of Embolus in Lower Extremities

Site	State of pulsations	Oscillometric readings	Reduction of skin temp	Color changes	Anesthesia or hypesthesia	Other neurologic findings	Treatment of choice
Bifurcation of aorta	No pulsations in either femoral artery or in any of the vessels in the 2 limbs	Zero readings at all levels on both lower extremities including upper thighs	Marked coldness of both feet legs and most of the thighs up to groins	Marked pallor of both feet and legs at times extending onto thighs mottled irreversible cyanosis in feet and elsewhere including lower abdominal wall	Anesthesia of feet and lower portion of legs hypesthesia may extend up on thighs	Bilateral foot drop and motor paralysis of toes	Embolectomy followed by conservative therapy
Common iliac artery	No pulsations in femoral artery or below this level on involved side normal side may show some reduction in pulsations due to spasm	Zero readings at all levels including upper thigh in involved extremity normal readings on opposite extremity or reduced ones if vasospasm exists	Marked coldness of foot leg & thigh to mid portion	Marked pallor of involved foot extending onto leg and even thigh cyanosis of foot and elsewhere including lower abdominal wall on affected side	Anesthesia of foot and leg hypesthesia above knee	Frequently foot drop on involved side & inability to move toes knee movements weak or absent	Embolectomy followed by conservative therapy
Iliofemoral artery	No pulsations in femoral artery or below this level on involved side reduced or normal pulsations on other side depending on whether or not spasm is present	Zero readings at all levels including upper thigh normal pulsations on opposite limb	Marked coldness of foot leg & lower part of thigh	Definite pallor of foot and leg with some extension onto thigh cyanosis of toes and legs	Anesthesia of foot and lower part of leg hypesthesia of rest of leg	Possibly foot drop on involved side and some loss of motor power in toes	Embolectomy followed by conservative therapy

cubital space and normal or even increased oscillometric readings are obtainable *from the lower portion of the arm*

Occlusion of either the radial or ulnar artery is a rare finding and when present is associated with minimal signs such as some reduction in skin temperature of the fingers In most instances no obvious neurologic changes are observed The diagnosis is made primarily on the sudden appearance of pain in a portion of a hand, slight color changes and absent *pulsations in the involved vessel at the wrist*

Treatment

Prophylaxis

As in pulmonary embolism, the most important part of therapy in arterial embolism is prophylaxis Although in general this is much more difficult to achieve than in the case of venous thrombosis several proposed approaches are *worthy of further clinical trial*

Anticoagulant Therapy in Myocardial Infarction Whether or not the recently established plan for the early use of anticoagulants in the treatment of myocardial infarction will reduce the possibility of formation of mural thrombi in the left ventricle, and hence peripheral emboli can only be determined through long range investigations On purely theoretical grounds and on the basis of existing reports the results suggest that there may be some value to the method

Mitral Commissurotomy and Appendectomy In addition to the major aim *of increasing the efficiency of the heart and lowering pulmonary pressure, mitral* commissurotomy has been considered of value in decreasing the incidence of peripheral embolism This is believed to result from the fall in left atrial pressure followed by a reduction in size of the chamber, a change which tends to minimize the formation of thrombi The simultaneous removal of the left atrial appendage by eliminating a potential site for the collection of thrombi theoretically, at least contributes to the same aim Unfortunately many more years of investigation are necessary before the efficacy of these operations in the *prevention of embolic episodes can be determined*

Steps to Control or Alter Existing Rhythm of the Heart Whether or not the re-establishment of a normal sinus rhythm in a patient with long standing auricular fibrillation carries the risk of liberating pieces of clots from the left atrium into the peripheral circulation has never been satisfactorily determined Auricular fibrillation itself appears to predispose to the formation of emboli although the same process can also occur in the presence of a normal sinus rhythm provided the left atrium is markedly dilated and stasis is present However the situation most fraught with danger is the one in which there are repeated transitions from one type of rhythm to another If such changes occur spontaneously the best policy is to maintain by means of appropriate medications the existing conditions observed at the time *of the first examination*

Treatment of Acute Phase

Once the diagnosis *of arterial embolism has been made and the site of occlusion* determined therapy should be instituted immediately This consists of several

Table 14 Location of Site of *Embolus* in Lower Extremities

Site	*State of pulsations*	*Oscillometric readings*	*Reduction of skin temp*	*Color changes*	*Anesthesia or hypesthesia*	*Other neurologic findings*	*Treatment of choice*
Bifurcation of aorta	No pulsations in either femoral artery or in any of the vessels in the 2 limbs	Zero readings at all levels on both lower extremities including upper thighs	Marked coldness of both feet legs and most of the thighs up to groins	Marked pallor of both feet and legs at times extending onto thighs mottled irreversible cyanosis in feet and elsewhere including lower abdominal wall	Anesthesia of feet and lower portion of legs hypesthesia may extend up on thighs	Bilateral foot drop and motor paralysis of toes	Embolectomy followed by con servative therapy
Common iliac artery	No pulsations in femoral artery or below this level on in volved side normal side may show some reduc ion in pulsa tions due to spasm	Zero readings at all levels including upper thigh in in- volved extrem ity normal readings on opposite ex- tremity or reduced ones if vasospasm exists	Marked coldness of foot leg & thigh to mid portion	Marked pallor of involved foot extend ing onto leg and even thigh cyanosis of foot and elsewhere including lower abdominal wall on affected side	Anesthesia of foot and leg hypesthesia above knee	Frequently foot drop on in volved side & in ability to move toes knee move- ments weak or absent	Embolectomy followed by con- servative therapy
Iliofemoral artery	No pulsations in femoral artery or below this level on in- volved side reduced or nor- mal pulsations on other side depending on whether or not spasm is present	Zero readings at all levels including upper thigh normal pulsa- tions on opposite limb	Marked coldness of foot leg & lower part of thigh	Definite pallor of foot and leg with some extension onto thigh cyanosis of toes and legs	Anesthesia of foot and lower part of leg hypesthesia of rest of leg	Possibly foot drop on in- volved side and some loss of motor power in toes	Embolectomy followed by con servative therapy

Table 14 (continued)

Site	*State of pulsations*	*Oscillometric readings*	*Reduction of skin temp*	*Color changes*	*Anesthesia or hypesthesia*	*Other neurologic findings*	*Treatment of choice*
Bifurcation of femoral artery	Normal or increased pulsations in femoral artery at Poupart s ligament and none below this level normal pulsations on other side	Normal or somewhat increased readings may be present in *upper thigh* but zero readings on lower thigh and all levels below this normal readings on opposite limb	Marked coldness of foot and leg up to knee	Definite pallor of foot and leg extending to knee cyanosis of toes	Anesthesia of foot and adjoining portion of leg hypesthesia of lower part of leg	Possibly foot drop on involved side and inability to move toes ankle movements absent or diminished	Embolectomy and/or conservative *therapy*
Full length of popliteal artery	Normal pulsations in femoral artery down to its bifurcation none below this level normal pulsations *on* opposite sides	Normal or increased readings on both levels on thigh but zero readings at levels below knee	Definite coldness of foot and *lower part* of leg	Definite pallor of foot and lower part of leg	Anesthesia of foot and hypesthesia of lower part of leg	Motor power weak or *absent* in toes	Embolectomy followed by conservative therapy
Bifurcation of popliteal artery	Normal pulsations in femoral increased pulsations in popliteal none below this level normal pulsations on opposide side	Normal readings on thigh reduced readings just below knee with zero readings above ankle	Some coldness in foot	Some pallor of foot	Possibly some hypesthesia of foot	Generally only minor change	Conservative therapy

Table 14 *(continued)*

Site	*State of pulsations*	*Oscillometric readings*	*Reduction of skin temp*	*Color ch nges*	*Anesthesia or hypesthesia*	*Other neurologic findings*	*Treatment of choice*
Anterior tibial artery	Normal or some hat reduced pulsations in all vessels but *dorsalis pedis* none in latter normal pulsa tions on opposite side	Normal readings on thigh re duced readings at calf and above ankle	Slight coldness on dorsum of foot	Slight pallor of toes or no change	None	Generally none	Conserv- ative therapy
Posterior tibial artery	Normal or some- what reduced pulsations in all vessels but posterior tibial *none in* latter normal pulsations on opposite side	Normal readings on thigh re duced readings at calf and above ankle	Slight coldness on plantar surface of foot	Slight pallor of sole of foot & toes or no change	None	Generally none	Conserv- ative therapy

Table 14 (continued)

Site	State of pulsations	Oscillometric readings	Reduction of skin temp	Color changes	Anesthesia or hypesthesia	Other neurologic findings	Treatment of choice
Bifurcation of femoral artery	Normal or increased pulsations in femoral artery at Poupart s ligament and none below this level normal pulsations on other side	Normal or somewhat increased readings may be present in upper thigh but zero readings on lower thigh and all levels below this normal readings on opposite limb	Marked coldness of foot and leg up to knee	Definite pallor of foot and leg extending to knee cyanosis of toes	Anesthesia of foot and adjoining portion of leg hypesthesia of lower part of leg	Possibly foot drop on involved side and inability to move toes ankle movements absent or diminished	Embolectomy and/or conservative therapy
Full length of popliteal artery	Normal pulsations in femoral artery down to its bifurcation none below this level normal pulsations on opposite sides	Normal or increased readings on both levels on thigh but zero readings at levels below knee	Definite coldness of foot and lower part of leg	Definite pallor of foot and lower part of leg	Anesthesia of foot and hypesthesia of lower part of leg	Motor power weak or absent in toes	Embolectomy followed by conservative therapy
Bifurcation of popliteal artery	Normal pulsations in femoral increased pulsations in popliteal none below this level normal pulsations on opposide side	Normal readings on thigh reduced readings just below knee with zero readings above ankle	Some coldness in foot	Some pallor of foot	Possibly some hypesthesia of foot	Generally only minor change	Conservative therapy

Table 14 (continued)

Site	*State of pulsations*	*Oscill metric readings*	*Reduction of skin temp*	*Color changes*	*Anesthesia or hypesthesia*	*Other neurologic findings*	*Treatment of choice*
Anterior tibial artery	Normal or some what reduced pulsations in all vessels but dorsalis pedis *none in latter normal pulsa tions on* opposite side	Normal readings on thigh re duced readings at calf and above ankle	Slight coldness on dorsum of foot	Slight pallor of toes or no change	None	Generally none	Conserv-ative therapy
Posterior tibial artery	Normal or some-what reduced pulsations in all *vessels* but *posterior* tibial - none in latter normal pulsations on opposite side	Normal readings on thigh re duced readings at calf and above ankle	Slight coldness on plantar surface of foot	Slight pallor of sole of foot & toes or no change	None	Generally none	Conserv ative therapy

approaches all of which should be utilized simultaneously Their common aim is to restore the blood flow through the obstructed artery, or if this is impossible, to encourage the establishment of an adequate collateral circulation Unfortunately, in some instances neither goal can be achieved and under such circumstances permanent ischemia occurs, thus leading to gangrene and the necessity of amputation However, since frequently one can not predict such an outcome early in the disease it is essential that all cases be diligently treated except when frank trophic disturbances are already present

Medical Therapy

Use of Anticoagulants The first step is the institution of anticoagulant therapy to prevent propagation of the clot into other segments of the involved vessel and its branches This is carried out according to the plan outlined in *Combined Administration of Heparin and Dicumarol*, Chapter XXIX

Procedures for Removal of Vasomotor Tonus The next approach begun at the same time, involves means for removing vasospasm from the collateral vessels Of advantage in this regard are vasodilating drugs such as papaverine, given very slowly intravenously in doses of 32 to 65 mg (½–1 gr) and the sympathetic blocking agents administered either intramuscularly or intravenously The most commonly used of the latter are Priscoline 25–75 mg Hydergine 0 3 mg (1 cc), and bistrium bromide 50–75 mg (2–3 cc) * The medications may be repeated every 4 to 8 hours depending upon the response of the patient In the lower extremity if the femoral artery is patent these drugs may be given intra arterially since in this manner the full vasodilating effect is exerted locally on the vessels in spasm [7] Other medical procedures of value are the application of heat to distant portions of the body and whisky by mouth both of which produce indirect vasodilatation in the involved limb Procaine, 1000 cc of 0 1% in 5% glucose in water administered intravenously is also useful since it reduces pain perception† through its anesthetic effect at the same time that it has some inhibitory *action on vasomotor tonus*

Blocking of the peripheral sympathetic fibers is also frequently utilized in removal of spasm from the collateral vessels However repeated paravertebral sympathetic blocks are contraindicated if the patient is under the effect of anticoagulants since massive hematomas may be produced under these circumstances (p 446) The *substitution of a continuous block of the sympathetic ganglia* using a spinal catheter is not as dangerous in this regard since the measure permits the regulation of the duration of the inhibitory effect while with a paravertebral sympathetic block the change may last only for an hour or so and hence the procedure must be repeated Continuous spinal or caudal anesthesia also produces *prolonged sympathetic block Both have the advantage of* simultaneously controlling the severe pain that accompanies ischemia of tissue (For further discussion, see *Continuous Blockade of Paravertebral Sympathetic Ganglia* Chap XXVII)

* The pharmacologic action of these drugs is described in *Ganglionic blocking agents* and *Adrenergic blocking agents* Chap XXX

† For the control of the severe pain opiates should be used freely

Local Therapy The involved extremity should be wrapped in several layers of cotton padding to form a boot In this way the warmth arising from the small quantity of blood circulating through it is conserved and at the same time the limb is protected from pressure The local application of heat is contraindicated inasmuch as it may precipitate gangrene (Fig 19) while cold although reducing metabolic needs also has a detrimental effect because it produces marked vaso constriction

The affected limb should be placed slightly below heart level by raising the head of the bed about 20 cm (8 inches) since in this manner local arterial blood flow is somewhat increased At no time should the extremity be maintained in an elevated position



FIG 19 *Third degree burn produced by the application of a heating pad to the leg following embolism to femoral artery*

Embolectomy

Although the consensus is in favor of most of the steps described above there is considerable difference of opinion regarding the advisability of simultaneous embolectomy Some investigators believe that conservative therapy should always be utilized irrespective of the site of occlusion while others consider surgical removal of the embolus to be the first step in treatment in most instances On the basis of personal experience and of a review of the results reported in the literature the following plan appears warranted

Occlusion of any of the main arteries of the upper extremity of the bifurcation of the popliteal artery and of either the anterior or posterior tibial artery should generally be treated conservatively On the other hand with lodgment of an embolus at the bifurcation of the aorta in the common iliac in the iliofemoral (Fig 18) at the bifurcation of the femoral and in the popliteal artery for its full length embolectomy is the method of choice provided the following criteria can be met

Criteria for Embolectomy The surgeon should be capable of performing the operation with facility and celerity Furthermore the diagnosis must have been made early enough to permit the procedure to be carried out before 8–10 hours have elapsed from the inception of the condition for otherwise the arterial tree

approaches, all of which should be utilized simultaneously Their common aim is to restore the blood flow through the obstructed artery, or if this is impossible, to encourage the establishment of an adequate collateral circulation Unfortunately, in some instances neither goal can be achieved, and under such circumstances permanent ischemia occurs, thus leading to gangrene and the necessity of amputation However, since frequently *one can not predict such an outcome* early in the disease, it is essential that all cases be diligently treated except when frank trophic disturbances are already *present*

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* The pharmacologic action of these drugs is described in *Ganglionic blocking agents* and *Adrenergic blocking agents* Chap XXX

† For the control of the severe pain opiates should be used freely

may disappear In most of the successful cases however the results are not so spectacular The color changes and the rise in cutaneous temperature may be delayed for several days probably because of local spasm of the artery following operative trauma or a similar process in the collateral vessels initiated by the original condition Arterial pulsations may not be felt until later or in some patients they may never return

When embolectomy fails to prevent the appearance of nutritional disturbances the sequence of events is similar to that observed in the unsuccessful case after the use of conservative measures This type of response may be due to the subsequent formation of a thrombus at the operative site to occlusion of the distal branches by a clot which had propagated into them and which was inaccessible from the opening in the involved vessel or to thrombosis of these channels as a result of prolonged spasm

TREATMENT OF THE LATER PHASE

Regardless of whether or not embolectomy is performed certain therapeutic procedures should be carried out until the situation has become stabilized These consist of the continued use of dicumarol and of the various measures to maintain vasomotor paralysis However as soon as it is clear that the viability of the distal portion of the limb has been preserved the medications are discontinued and the patient is permitted to become ambulatory If recovery is not complete and there is a foot drop this should be treated by the use of a foot brace and intensive physical therapy The frequent symptoms of irritation of peripheral nerves such as lancinating pain burning and paresthesias are difficult to control although at times they may respond to the oral administration of large doses of thiamine chloride (200 mg four times a day)

If therapy has not been successful and there is frank gangrene of the toes and adjoining portion of the foot anticoagulants should be discontinued and the patient prepared mentally (p -1-) and physically for amputation Although it is generally advisable to allow the prothrombin activity in the blood to return to a normal level before performing surgery if immediate removal appears indicated because of absorption from the gangrenous site the hypoprothrombinemia should be rapidly corrected by the intravenous administration of natural vitamin K_1 oxide However systemic reactions can also be controlled by refrigeration of the distal portion of the limb Such a measure can be prolonged until the time is more propitious for surgery without any particular increase in risk to the patient (p 14)

LONG RANGE TREATMENT PROGRAM

With control of the acute episode of arterial embolism the question arises as to how to prevent a repetition If the mechanisms responsible for the first attack continue to operate one can expect new thrombi to be liberated into the blood stream with perhaps disastrous results should the occlusion occur in such vital sites as the brain or abdominal viscera rather than in the extremities A proposal which has been made for dealing with the problem is the continued use of long acting anticoagulants to minimize the growth of new clots at the original source

distal to the embolus becomes occluded with propagating thrombus The only exception to this rule is the occurrence of an embolus at the bifurcation of the aorta or of the common iliac artery (Fig 18 A and C) Because of the practically hopeless outlook associated with conservative treatment, embolectomy is the proper procedure even when the interval is as long as 18 hours In all instances if the patient had been started on heparin then a delay in operation is not as serious for further growth of the thrombus should be prevented on such a regimen

The final requirement is that the patient s general condition is such that he is capable of withstanding surgical treatment In the case of an embolectomy performed on the femoral or popliteal artery the operative risk is minimal inasmuch as a local anesthetic is utilized However, for exposure of the aorta or of the common iliac artery the danger is much increased since the abdomen must be entered requiring a general or spinal anesthetic As a rule then it can be stated that the elderly patient with generalized arteriosclerosis and arteriosclerotic heart disease is a much less ideal subject for embolectomy than the young individual with rheumatic heart disease

In the case of an embolus lodged in the popliteal artery certain other factors must be evaluated before considering embolectomy If the individual is 50 years of age or over, surgical removal of the clot is attended with such technical difficulties that the possibility of a successful outcome is small[3] This is due to the fact that patients in the older age groups frequently manifest severe atheromatous changes in the popliteal artery which make repair of the arteriotomy almost impossible Even if this is accomplished the site of operation is a focus for post operative thrombosis Such objections do not apply to younger individuals

General Precautions in Performing an Embolectomy The fact that most patients are already under the effect of heparin at the time embolectomy is contemplated should play little role in altering this decision However such a situation does require the observance of meticulous hemostasis before the wound is closed, since otherwise hematomas may develop In operations on the aorta the common iliac and the iliofemoral arteries, the matter of postoperative bleeding is of greater consequence for it can not be readily recognized or controlled

If vasodilating procedures are used as a preliminary to embolectomy certain possibilities must be kept in mind Such measures may cause sufficient relaxation of the artery to allow the embolus to escape from its original site and occlude a smaller vessel or to enter one not easily accessible to surgical intervention Furthermore they may remove the superimposed and masking effect of vaso spasm thus making more obvious those findings which point to the actual site of occlusion As a general rule therefore the involved extremity should be re-examined for localizing signs perhaps just before it is prepared for operation

Types of Results Following Embolectomy Once the embolus is removed certain changes can be expected to occur in the foot and leg In some instances there is an immediate re-establishment of the circulation which manifests itself in a return of normal color cutaneous temperature and pulsations on occasion occurring while the patient is still in the operating room The pain may subsequently cease and such neurologic signs as foot drop and paralysis of the toes

or that the neurologic changes are not more pronounced By the third day however in order to continue having a basis for optimism there should be some definite findings to indicate that the circulation is becoming adequate Significant in this regard are a lowering of the levels of reduced cutaneous temperature and of anesthesia or hypesthesia renewed ability to move some of the toes and to dorsiflex the foot a return of normal skin color to the leg and even part of the foot and slightly more prominence of the previously collapsed superficial veins

If instead of the above clinical picture the day after occlusion there are definite signs of progression of the ischemic process the prognosis is much poorer Of special importance in this regard is a greater degree of apparently cyanotic mottling of the foot and lower portion of the leg which is not blanched by digital pressure When the change is present on the leg alone it does not have so serious a connotation If the changes in the color of the foot are associated with wrinkling of the skin of the toes due to absorption of fluid from the tissues there is further support for the belief that the limb is in a state of impending gangrene At times however such a response is reversible provided the process has not progressed too far A rise in the level of anesthesia and complete paralysis of the toes are also bad prognostic signs Generally if all these findings persist for 48 hours dry gangrene of the toes can be expected to make its appearance soon afterward

LOCAL SEQUELAE AND COMPLICATIONS

If nutritional disturbances do not occur and the extremity is saved the future course will depend upon the amount of blood flowing through the main arterial channels and the efficiency of the collateral vessels In the presence of a circulation which is adequate for the metabolic needs of the tissues with activity as well as with rest the patient s clinical status will be no different from that present before embolism

However in many instances the compensatory mechanisms are not effective enough and as a result severe weakness and intermittent claudication in the limbs may be experienced With a marked impairment in blood supply the nutrition of the skin may suffer thus predisposing the limb to ulceration or gangrene Neurologic abnormalities as for example foot drop may persist for months after the acute stage has subsided and in some cases may even be permanent The results of nerve irritation such as burning numbness and paresthesia are frequently relatively temporary complaints In general it can be stated that the sequelae of embolism are more severe following conservative treatment of the acute stage of this condition than after embolectomy

ARTERIAL THROMBOSIS

ETIOLOGIC FACTORS

Thrombosis of arterial channels in the limbs may be the result of a variety of different agents but particularly disease processes Among the latter are the inflammatory disorders such as thromboangiitis obliterans polyarteritis nodosa

However, a number of practical objections arise regarding this plan the first being the cost of continuous testing necessary to control the prothrombin level Once the maintenance dose of the anticoagulant has been determined by trial and error, it is true that the number of prothrombin tests per week can generally be reduced to three or two or even one Still with this arrangement a certain amount of risk always exists, because minor conditions such as an upper respiratory infection may be enough to alter the prothrombin activity of the blood with the result that now the established dosage may either cause bleeding or be ineffective in preventing new emboli from forming Because of such possibilities, a patient on anticoagulant therapy must be under continuous medical supervision, which few can afford Theoretically, at least this must be maintained for the remainder of the patient's life, which complicates the situation even further

In view of all these objections, a decision to place a patient on such a regimen must be arrived at after due consideration of many factors other than its possible medical efficacy Only in the occasional individual, in unusual circumstances is the plan applicable (For a discussion of the value of removal of the left atrial appendage in the prevention of embolic phenomena see p 154)

PROGNOSIS

The prognosis in arterial embolism depends upon the vessel occluded the degree of vasospasm the effectiveness of the therapeutic procedures in removing it, and the rapidity with which the collateral circulation readjusts itself to the greater burden placed upon it

Significance of the Site of Occlusion There is little question that complete obstruction of some of the large arteries in the extremities carries an excellent prognosis while the same process in others almost invariably results in gangrene despite intensive therapy Although involvement of the vessels in the upper extremity is usually much less serious than of those in the lower still on occasion nutritional disturbances may occur there With regard to the lower extremity the very poor prognosis associated with obstruction of the bifurcation of the aorta and the common iliac artery has already been mentioned The same applies to occlusion of the entire popliteal artery However if the obstruction is limited to the bifurcation of this vessel so that the genicular branches can function the outlook is greatly improved Occlusion of the femoral artery at its bifurcation carries a somewhat better prognosis than in the case of complete involvement of the popliteal artery Obstruction of either the anterior tibial or the posterior tibial artery ordinarily causes no serious untoward effects

Clinical Course as an Index of Prognosis Considerable information regarding the outcome can be obtained by observing the changes which occur in the involved limb early in the acute phase of arterial embolism If by the second day the pain is the same or less, the neurologic findings have not become more severe and the cyanosis of the toes and foot is still reversible the possibility of preserving the limb is increased Naturally in the presence of recession in any of the symptoms or signs even if only minimal this belief is strengthened When no obvious improvement is apparent after 48 hours from onset there is still a good possibility that the foot will be saved provided that irreversible cyanosis has not developed

and mycotic arteritis the infectious diseases (Fig 20A), and the degenerative conditions as typified by arteriosclerosis obliterans Simple arterial thrombosis may also exist with little or no histopathologic changes in the involved vessels (*essential thrombophilia*) [8] Another etiologic group consists of arterial thrombosis produced by trauma (For pathogenesis of the latter see *Traumatic Arterial Thrombosis* Chap XVII)

CLINICAL MANIFESTATIONS

General Considerations

Arterial thrombosis presents itself clinically in two forms depending upon the rate of occlusion If the process occurs rapidly the changes resemble the dramatic episode of arterial embolism since in both the underlying mechanism is



FIG 1 Saddle thrombus at bifurcation of aorta associated with marked atheromatous changes in proximal portion of vessel (Leriche s syndrome)

sudden ischemia of tissues If a diseased artery is the site of obstruction as in arteriosclerosis obliterans or thromboangiitis obliterans the clinical picture is generally not as marked or as clear-cut since the previous existence of a slowly growing collateral circulation helps counteract to some extent the acute anoxia ushered in by the sudden and now complete thrombosis of the vessel Nevertheless there may be symptoms and signs of impaired nutrition to peripheral nerves in the form of pain numbness and tingling of the digits a stocking glove type of anesthesia or hypesthesia foot drop and paralysis of the small muscles of the foot Peripheral signs of a markedly impaired arterial circulation such as absence of pulsations and oscillometric readings below a given level pallor and mottled cyanosis of the skin and a low cutaneous temperature are also frequently noted

In the second type of arterial thrombosis the process forms so slowly that there is generally sufficient time for new collateral vessels to take over the function of supplying the tissues with nutrition As a consequence even when complete occlusion occurs there are very few symptoms except possibly the [illegible] intermittent claudication Physical examination however usually reveals [illegible] of involvement of the main artery such as absence of pulsation [illegible]



Fig 20 A Gangrene of first and second toes due to thrombosis of small arteries in the foot associated with trichinosis



Fig 20 (*Continued*) B Gangrene of foot following thrombosis of a popliteal arterial aneurysm Clear line of demarcation noted

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Clinical Manifestations

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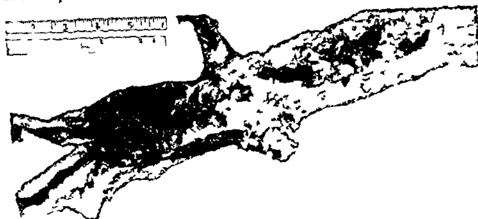


Fig 21 Saddle thrombus at bifurcation of aorta associated with marked atheromatous changes in proximal portion of vessel (Leriche s syndrome)

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metric readings Nevertheless the various tests for circulatory efficiency, such as the plantar pallor test, the venous filling time, and time of return of color (Chaps II and III), generally are found to be only somewhat abnormal thus indicating that an adequate circulation through collateral vessels exists despite the absence of blood flow through the main arterial tree

Characteristics of Specific Clinical Entities

Insidious Thrombosis of Aortic Bifurcation A disorder which does not have its clinical counterpart in arterial embolism is the gradual thrombotic obliteration of the terminal portion of the aorta, known as Leriche s syndrome (Fig 21)[5,6] The underlying mechanism is atheromatous formation* which generally begins in one of the common iliac arteries and extends upward into the aorta, hampering the blood flow to the opposite side but not stopping it entirely for some time Ultimately the result is occlusion of both iliacs *and the aortic bifurcation*, as a result of narrowing due to atheromatous formation with superimposed thrombosis Less frequently the process originates in the aorta and progresses downward into the iliacs Usually there is an extensive periarteritis which attaches the thrombotic segment of the aorta to the surrounding tissues particularly the inferior vena cava

Because of the extremely slow rate of obstruction that occurs in this condition the marked changes generally associated with a sudden and complete occlusion of a main arterial channel are absent At first the disorder was considered to occur more commonly in males but this view is not substantiated by recent reports In the male the first sign may be inability to maintain an erection, apparently due to an insufficient supply of blood to fill the cavernous portion of the penis and eventually permanent sexual impotency Other findings consist of extreme fatigue of both lower extremities, even *on standing intermittent claudication* particularly in the hips and thighs local muscle atrophy a low cutaneous temperature and pallor of the feet absence *of all pulses in both lower limbs and no oscillometric* readings even high on the thigh However pulsations can be felt in the aorta above the level of the umbilicus a differential point from coarctation of the aorta in which none is noted along the entire abdominal course of the vessel Translumbar arteriography is of considerable value in establishing the diagnosis of Leriche s syndrome in the less typical case

Nutritional changes are generally not observed early in the disease but after 5 to 10 years they may appear probably as a result of proximal propagation of the thrombus producing occlusion of the orifices of the collateral vessels The first signs of such alterations may be the onset of edema and a general violaceous hue to the leg followed by ecchymosis ulcers on all pressure points and finally, gangrene not necessarily bilateral

Thrombosis Secondary to Aneurysm of Popliteal Artery Although all arterial aneurysms are potential sites for thrombosis such a lesion of the popliteal artery is particularly susceptible The dilated portion of the vessel is frequently filled

* Occasionally syphilis inflammatory disorders of the peritoneum and sequelae of deep x ray therapy to the abdomen may produce a similar type of clinical entity

with a laminated clot that may act as a focus for further growth into the lumen A reduction in blood flow through the patent portion accelerates the process The thrombus may continue to enlarge until the entire artery is occluded which generally leads to loss of viability of the tissues of the foot and gangrene (Fig 0B) unless the rate of occlusion has been slow enough to permit the development of an adequate collateral circulation

TREATMENT

THERAPY IN THE ACUTE PHASE

The treatment of the acute stage of arterial thrombosis is similar in all regards to that described for arterial embolism except that embolectomy is not utilized Procedures to remove vasospasm of collateral vessels should be instituted at once together with the combined use of heparin and dicumarol to prevent propagation of the thrombus The local treatment of the limb likewise includes attempts to conserve its own heat without increasing the metabolic needs of the tissues

As in the case of arterial embolism if gangrene occurs despite treatment amputation of the limb should be preceded by discontinuation of the anticoagulants so as to allow the prothrombin content of the blood to reach a normal level If it is necessary to operate before this can be achieved then natural vitamin K_1 oxide should be given to facilitate the reversal

Removal of the clot is not indicated in the acute stage of arterial thrombosis because of the danger of recurrence of the process due to surgical injury of the intima Moreover since the underlying mechanism is frequently atherosclerosis the subsequent repair of the vessel would also present a problem In fact in some instances it has been found necessary to ligate the artery because complete closure could not be achieved

THERAPY IN THE LATER PHASE

A surgical approach of some promise which can be used in the chronic stage of arterial thrombosis is resection of the portion of artery containing the thrombus and replacement with a similar sized segment of vein This is of value only when the pathologic change consists of a segmental involvement with the rest of the vessel demonstrating a relatively normal-sized lumen It is therefore essential first to perform an arteriogram using 70% Diodrast in order to outline the lumen of the vessel and its collateral channels and to determine the exact location of the thrombus (For the technic of procedure see Chap XXV)

Another surgical procedure utilized in the treatment of thrombosed segments of main arteries consists of resecting the intima and diseased portion of the media together with the thrombus the feasibility of the measure depending upon the existence of a pathologic cleavage plane within the media The length of artery successfully treated by this method of thromboendarterectomy has been reported to be as much as 48 cm (approximately 20 inches)[1] It is necessary to point out however that there may be two complications of such an operation aneurysmal dilatation of the weakened artery and inadequate closure of the incision because of poor structure of the remaining vessel wall The latter may pro

metric readings Nevertheless the various tests for circulatory efficiency such as the plantar pallor test the venous filling time and time of return of color (Chaps II and III), generally are found to be only somewhat abnormal thus indicating that an adequate circulation through collateral vessels exists despite the absence of blood flow through the main arterial tree

Characteristics of Specific Clinical Entities

Insidious Thrombosis of Aortic Bifurcation A disorder which does not have its clinical counterpart in arterial embolism is the gradual thrombotic obliteration of the terminal portion of the aorta known as Leriche's syndrome (Fig 21) [6] The underlying mechanism is atheromatous formation* which generally begins in one of the common iliac arteries and extends upward into the aorta hampering the blood flow to the opposite side but not stopping it entirely for some time Ultimately the result is occlusion of both iliacs and the aortic bifurcation as a result of narrowing due to atheromatous formation with superimposed thrombosis Less frequently the process originates in the aorta and progresses downward into the iliacs Usually there is an extensive periarteritis which attaches the thrombotic segment of the aorta to the surrounding tissues particularly the inferior vena cava

Because of the extremely slow rate of obstruction that occurs in this condition the marked changes generally associated with a sudden and complete occlusion of a main arterial channel are absent At first the disorder was considered to occur more commonly in males but this view is not substantiated by recent reports In the male the first sign may be inability to maintain an erection, apparently due to an insufficient supply of blood to fill the cavernous portion of the penis and eventually permanent sexual impotency Other findings consist of extreme fatigue of both lower extremities even on standing intermittent claudication particularly in the hips and thighs local muscle atrophy a low cutaneous temperature and pallor of the feet absence of all pulses in both lower limbs and no oscillometric readings even high on the thigh However pulsations can be felt in the aorta above the level of the umbilicus a differential point from coarctation of the aorta in which none is noted along the entire abdominal course of the vessel Translumbar arteriography is of considerable value in establishing the diagnosis of Leriche's syndrome in the less typical case

Nutritional changes are generally not observed early in the disease but after 5 to 10 years they may appear probably as a result of proximal propagation of the thrombus, producing occlusion of the orifices of the collateral vessels The first signs of such alterations may be the onset of edema and a general violaceous hue to the leg followed by ecchymosis ulcers on all pressure points and finally gangrene, not necessarily bilateral

Thrombosis Secondary to Aneurysm of Popliteal Artery Although all arterial aneurysms are potential sites for thrombosis such a lesion of the popliteal artery is particularly susceptible The dilated portion of the vessel is frequently filled

* Occasionally syphilis inflammatory disorders of the peritoneum and sequelae of deep x ray therapy to the abdomen may produce a similar type of clinical entity

with a *laminated clot* that may act as a focus for further growth into the lumen A *reduction in blood* flow through the patent portion accelerates the process The thrombus may continue to enlarge until the entire artery is occluded which generally leads to loss of viability of the tissues of the foot and gangrene (Fig 20B) unless the rate of occlusion has been slow enough to permit the development of an adequate collateral circulation

Treatment

Therapy in the Acute Phase

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gangrene of the toes and foot (Fig 20B) while occlusion of the anterior tibial or posterior tibial artery rarely results in such changes Complete obstruction of the *femoral* artery above its bifurcation may or may not cause nutritional disturbances depending upon the other factors previously enumerated

Compared with embolism of the bifurcation of the aorta thrombosis in this site has a much better outlook provided the process is slow and enough time is present for the formation of an adequate circulation However in most instances *the untreated cases will* ultimately show signs of gangrene in one or both lower extremities Furthermore if the process should extend upward to and above the orifices of the renal arteries uremia and death will follow



FIG 20 A Gangrene of foot and adjoining portion of leg following thrombosis of an aneurysm of the left common iliac with extension of the process into the external iliac artery B Gangrene of foot and leg produced by thrombosis of the femoral artery following prolonged vomiting and diarrhea in a patient susceptible to intravascular clotting

DIFFERENTIAL DIAGNOSIS OF ARTERIAL OCCLUSION

Distinguishing Points between Arterial Embolism and Thrombosis Of importance in this regard is a careful history with special emphasis on determining whether such a symptom as intermittent claudication suggesting the presence of a chronic occlusive arterial vascular disease had been present before the acute episode The existence of signs of an impaired local blood flow in the past as recorded in an examination would also favor the diagnosis of arterial thrombosis However it is necessary to point out that on occasion the first clinical indication of a long standing organic arterial disease may be the onset of complete obstruction of an arterial channel The presence of an associated condition conducive

duce hemorrhage which is difficult to control In order to counteract these tendencies, the use of fascia lata applied as a graft about the involved segment of artery has been suggested [11]

Where *segmental occlusion of the arteries of the lower extremities* can be demonstrated by arteriography, while the small vessels are still shown to be patent, removal of the thrombosed portion alone may on occasion be advisable However if the disease has progressed to the point of obliteration of branches also, this procedure is not indicated The rationale for resection without reconstruction of the continuity of the vessel is the belief that the thrombosed segment acts as a focus of irritability to initiate vasospasm in the remaining normal channels

With regard to Leriche s syndrome, several surgical approaches have been proposed Since the involved portion of aorta has also been considered capable of initiating distant spasm it has likewise been suggested that resection of the terminal segment of this vessel and of both iliacs should be carried out early in the disease,[8] preceded by a two stage bilateral sympathectomy However, for patients over 40 years of age with early trophic changes and muscular atrophy, this operation is inadvisable because of the associated extensive periaortitis generally present Propagation of the thrombus upward to the vicinity of the orifices of the renal arteries as determined by aortography is also a contraindication to resection Recently removal of the obstructed segment and replacement of the defect with a homologous artery graft has been proposed as another effective approach in *selected cases* [4, 9, 10]

Prognosis

Whether or not the limb can be saved after arterial thrombosis depends upon a number of factors primary among them being the state of efficiency of the collateral circulation when complete obstruction takes place If the process occurs as a terminal event in the course of a long standing arteriosclerosis obliterans then the possibility of the re establishment of an adequate blood flow is good However, even here there may be a period of local shock due to the fact that the mechanisms which ordinarily come into play under such circumstances must go through a state of readjustment in order to take on the full burden of supplying the metabolic needs of the extremity If this stage persists for any period of time *then gangrene will occur (Fig 22A)* *With a rapidly forming thrombosis* there may be insufficient collaterals built up by the time the process is complete As a result even measures for removal of all vasomotor tonus may not be effective in producing an adequate circulation through the existing patent channels (Fig 22B)

As in arterial embolism thrombosis of arteries in the upper extremities carries a better prognosis than *involvement of the main channels in* the lower However if the vessels involved are the main source of supply, as in the case of the digital arteries the end result may be the appearance of gangrene regardless of whether the location is in the fingers or toes This type of response is generally noted when the etiologic factor is an acute infectious disease

In the lower extremities *the location of the process influences* prognosis Involvement of the popliteal artery may be associated with the production of

gangrene of the toes and foot (Fig 20B) while occlusion of the anterior tibial or posterior tibial artery rarely results in such changes Complete obstruction of the femoral artery above its bifurcation may or may not cause nutritional disturbances depending upon the other factors previously enumerated

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to the formation of thrombi in the left side of the heart would tend to support arterial embolism as an etiologic agent for peripheral arterial occlusion as would a history of numerous embolic phenomena in other sites such as the brain spleen, and kidneys

A comparison of the clinical picture of the initial stage of the disease may also be helpful in differentiating arterial thrombosis from embolism although in many regards there is considerable similarity Of interest is the fact that *thrombosis of a large artery is not necessarily characterized by the sudden appearance of pain* as is usually the case with embolism and that there is a gradual rather than a sudden onset of numbness Still embolism may possess these findings if small particles of a cardiac clot enter the peripheral artery before the main occlusion occurs In general, the physical findings *are the same in both conditions, although* the degree of change is less in arterial thrombosis Whereas the signs of marked arterial embarrassment are usually limited to the involved extremity in arterial embolism, in arterial thrombosis changes indicative of chronic occlusive arterial vascular disease are frequently found in other limbs

Thrombosis of Deep Venous System in the Lower Extremity Little difficulty should ordinarily be encountered in differentiating arterial embolism or thrombosis in the lower extremity from obstruction of the main venous channel In the latter the presenting sign is edema of varying degree while in arterial occlusion if any thing the extremity appears thinner than normal due to a decrease in flow of blood *For the same reason the superficial veins are generally collapsed in con* trast to their distension in deep thrombophlebitis Furthermore, with venous in volvement pain and tenderness are experienced along the inner side of the thigh in the vicinity of the femoral vein and in the groin while arterial impairment is associated with symptoms in the distal portion of the limb and occasionally at the site of obstruction

Another differentiating point is the fact that in deep thrombophlebitis a systemic reaction occurs, in the form of malaise fever and a rise in white blood count and sedimentation rate On the other hand arterial occlusion does not elicit such a response *unless there is a rapid death of tissue with absorption of toxic material from the involved site (For summary of differential points* see Table 16 p 250)

One finding in deep thrombophlebitis which may mimic the clinical picture of arterial occlusion is vasospasm This may cause reduction or even complete dis appearance of the peripheral pulsations the presence of edema in the foot further *accentuating the difficulty of palpating the vessels A lowered skin temperature* cyanosis and even pallor may be other manifestations of vasospasm although the change in color may in part also be due to the stretching of the skin by the edema fluid Since in phlegmasia cerulea dolens actual gangrene may occur, this possibility must be kept in mind in the differential diagnosis of arterial occlusion *(For discussion of this clinical entity see Complications of acute stage* of non suppurative deep thrombophlebitis Chap XIV)

Vasospasm Due to Other Causes Vasospasm associated with causalgia post traumatic vasomotor disorders and related conditions (Chap VI) may on occasion be mistaken for arterial occlusion since these entities are frequently characterized

by severe pain in the distal portion of the involved limb However a careful history and examination are sufficient to make a differential diagnosis

Vasospasm due to trauma in the vicinity of an artery or to the vessel itself must also be distinguished from acute thrombosis or embolism An important feature in this state is the finding of a proximal border of pallid or mottled cyanotic area of skin which is irregular and not as sharply delineated as in organic arterial occlusion[2] Furthermore the pain muscular paralysis and anesthesia are not as great as would be expected on the basis of the degree and extent of the color changes in the skin

If the vasospasm is dependent upon the integrity of the sympathetic nervous system then the results following a paravertebral sympathetic block become diagnostic since under these circumstances there should be a rapid improvement in the clinical picture However if the changes are due to local spasm of the circular muscle fibers in the vessel wall temporary removal of vasomotor tonus will be ineffective It must always be remembered that if vasospasm persists for any length of time secondary thrombosis may result (For a discussion of vasospasm due to trauma see Acute Vascular Spasm Chap XVII)

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CHAPTER

XI VASCULAR ENTITIES PRIMARILY AFFECTING THE ARTERIAL TREE (*Continued*)

4 "COLLAGEN VASCULAR DISORDERS"

A number of vascular conditions are characterized by a widespread and extensive involvement of the blood vessels not only in the extremities but elsewhere in the body While in some like thromboangiitis obliterans and arteriosclerosis obliterans, the changes in the limbs are an important part of the clinical picture in others they are merely incidental to much more significant and serious abnormalities elsewhere Most of the latter fall into the group of so-called collagen vascular disorders [14] entities with diversified clinical manifestations but similar histologic changes Three of the most common of these generalized scleroderma polyarteritis nodosa and systemic lupus erythematosus will be presented below, while others are included in Chapter XXI devoted to rare vascular disorders since they are much less frequently seen in general practice

Before discussing the conditions it is necessary to review briefly the characteristics of collagen, a substance composed of intercellular material and cellular elements The intercellular material consists primarily of amorphous ground substance which can be recognized by deep staining with toluidine blue It is found most abundantly in mucous connective tissue Another component of intercellular substance is the collagen fibers probably arising from fibroblasts and laid down in the form of bundles The density and thickness of these fibers determine the variety of connective tissue formed The cellular elements consist of fibroblasts histiocytes mast cells pigment cells and fat cells

In the collagen disorders the characteristic histologic change is swelling of the intercellular ground substance of the connective tissue which now takes on the appearance of a granular material that stains pink with eosin and resembles fibrin Accompanying this are swelling degeneration and fragmentation of collagen fibers and degeneration of cellular elements To these alterations has been applied the term fibrinoid degeneration Generally there are also observed in such tissues varying degrees of proliferation and infiltration of leukocytes Besides widespread changes elsewhere the connective tissue in the walls of arteries and veins

is involved as well as the structures surrounding them As a result vascular lesions occur the clinical picture depending upon their location

It is necessary to point out that although fibrinoid degeneration is a common finding in collagen vascular disorders there is no evidence to indicate that the etiologic factor is similar in all these conditions In fact the collagen diseases can be considered to be etiologically heterogeneous[6] For this reason there is some question as to the basis for or the advisability of using such a designation

In some of the collagen diseases the pathogenesis has been considered to be a hypersensitivity of the connective tissues to bacterial and other proteins or to simple organic and inorganic compounds Antipneumococcic serum sulfonamides iodides and even sunlight have all been implicated It has also been suggested that the pathogenesis of the collagen disorders may in some way be related to hyaluronidase an enzyme which depolymerizes hyaluronic acid a component of the intercellular ground substance

SCLERODERMA (PROGRESSIVE SYSTEMIC SCLEROSIS)

General Considerations

Scleroderma is a generalized disorder of connective tissue of the skin subcutaneous tissue muscles fasciae tendons serous surfaces and internal organs Of importance in the field of peripheral vascular disorders is the fact that the connective tissue of blood vessels may likewise be affected Because of the widespread involvement frequently present there is some debate as to whether the term scleroderma should not be discarded and replaced by progressive systemic sclerosis[8]

Before discussing scleroderma it is necessary to define some of the expressions commonly employed to denote various aspects of this entity If the process is circumscribed and localized to small areas of the skin the condition has been designated as *morphea* However some doubt has been raised as to whether the pathogenesis in this condition is the same as in scleroderma *Generalized scleroderma* has been used by some workers as indicating a condition in which the changes are present primarily on the torso and proximal parts of both the upper and lower extremities although eventually the entire skin including that of the hands may become affected *Acrosclerosis* is a term applied to a condition manifesting similar skin changes but chiefly in the distal parts of the extremities (usually the hands and forearms) and preceded by episodes of vasomotor disturbances particularly Raynaud s syndrome Abnormalities are also present in the connective tissue in other parts of the body *

It is possible that there is no justification in arbitrarily setting up a classification of scleroderma since the different categories may merely be variations in the course of one disease However in its favor is the fact that such terminology permits localization of the pathologic conditions to certain sites

Incidence Scleroderma occurs in females twice as often as in males and most

* Sclerodactylia is also used to denote sclerodermatous changes in the extremities This state occurs secondary to long standing Raynaud s disease and is found in those digits repeatedly affected by the color change

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commonly in the fourth and fifth decades The condition is unusual before puberty With regard to the extremities *the most frequent involvement is in the* hands, with extension up the arms, while the legs and thighs are affected more rarely The disorder is only occasionally noted in the feet

Etiology *The cause of scleroderma is unknown, although it has been ascribed* to infectious and toxic agents and also to neurogenic, endocrine, and vascular disturbances Despite the presence of calcinosis in the subcutaneous tissues in some patients, a disturbed calcium metabolism has not been implicated as a causative factor Occupation also appears to play no role in this regard

Pathology The predominant pathologic changes consist of fibrinous degeneration of the collagen bundles in the lower portion of the cutis and elsewhere, an increase in thickness and density and straightening of the fibers and compression of the cellular elements of the connective tissue Early in the disease the cutis and subcutis are edematous and infiltrated with moderate numbers of lymphocytes and mononuclear cells but as the lesion progresses these abnormalities disappear and the changes in the collagenous tissue dominate the picture As a secondary response the epidermal layer undergoes atrophy and rete pegs may be absent in places

The smaller arteries in the involved area manifest signs of degeneration associated with thickening of the intima as a result of the deposition of concentric layers of fibrous tissue This may lead to complete obliteration of the lumen and subsequent focal necrosis or the same type of change may follow organization of existing thrombi The other layers of the vessel may also demonstrate pathologic changes

Pathogenesis The main cause of vascular abnormalities in scleroderma is probably a mechanical blocking or strangulation of the vessels in the cutaneous and subcutaneous tissue [1] Such a response is particularly obvious in the fingers *The reduced skin temperature and pulsations in the digital arteries may be due to* the increased subcutaneous tissue pressure [2,6] which initially may arise above that of the normal capillary and venule Although permanent collapse of these minute *vessels is generally prevented by a building up of pressure in them from the* arteriolar side in certain areas this mechanism might not be adequate to counteract localized ischemia and atrophy

Clinical Characteristics

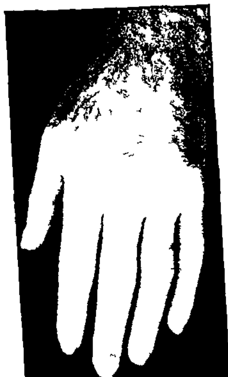
Changes in the Extremities

The manifestations noted in the limbs in scleroderma consist of changes in the state of the skin subcutaneous tissue and bone vasospastic phenomena nutritional disturbances and *deposition of calcium*

Sclerodermatous Changes The pathologic changes observed in the tissues of the limb can be divided into three stages The first consists of edema of the skin that may not be apparent because *it is generally of short duration* However on occasion it may last for weeks or months It is frequently symmetrical and often involves both the upper and lower extremities It may be associated with alterations in the periarticular tissues A low grade *fever may accompany the swelling* Tense

ness and stiffness of the skin and difficulty in using the fingers in fine movements, as in sewing, typing or playing the piano may appear gradually. Joint pain may be present as well as aching sensations in the muscles of the arm.

In the second phase permanent changes occur in the skin which becomes thickened, smooth and firm and feels like hard wax (Fig. -3). It can not be raised in a fold because of its adherence to the subcutaneous tissue. The normal wrinkling at the finger joints is lost since the skin is tightly stretched over all bony prominences. Pigmentation (deep brown to mahogany) of the affected sites is a common finding.





A B

FIG 3 Sclerodermatous changes in skin of hands. A Loss of normal wrinkling over joints. B Shiny appearance of skin with small ulceration at base of nail in third finger.

The last stage is characterized by atrophy of tissues (Fig -4). The fingers appear to be shorter than normal due to bony absorption of the terminal phalanges. Joint and tendon contractures may be noted producing inability to flex or extend the fingers and the typical clawlike appearance. As the sclerodermatous process advances it involves the backs of both the hands and forearms and the feet and legs. Atrophy of skeletal muscle in these sites may also take place primarily from disuse. Even in the far advanced case pulsations in the large peripheral arteries are generally normal.

X ray of the digits in the final stage usually reveals atrophy and absorption of the tufts of the terminal phalanges of the fingers The distal ends of the bones may be fragmented, forming sequestra with draining sinuses The subcutaneous deposits of calcium will also be visualized (see below)

Vasomotor Disturbances Such changes as hyperhidrosis, lowered cutaneous temperatures, and attacks of digital pallor elicited by exposure to cold (Raynaud s syndrome) may be noted, particularly in the case of acrosclerosis Persistent



Fig 24 Advanced stage of scleroderma demonstrating bony absorption of terminal phalanges and shortening of fingers (reproduced through the courtesy of Dr Samuel Silbert)

cyanosis is rarely noted since it is generally replaced by the characteristic pale waxlike skin The latter type of change is usually seen over the bony prominences when the hand is flexed

Nutritional Changes Commonly, there is a loss of subcutaneous fat which contributes to the characteristic pointed and atrophied appearance of the fingers The nails may become deformed shrunken and cracked As the sclerodermatous process continues a greater and greater reduction in local blood occurs in the distal portion of the digits so that slight trauma to such sites is frequently enough

to produce an ulcer (Fig 73B) The lesion is generally shallow indolent and associated with very little pain It is characteristically resistant to therapy

Calcinosis Subcutaneous nodules of calcium may be palpable in various sites and may be extruded through the skin in an ulcerative area These lesions designated as calcinosis appear to have a predilection for areas subjected to pressure such as the tips and plantar surface of the fingers the medial aspect of the arms the elbows and the skin over the tibia and in front of the patella It is possible that calcinosis has its origin in some type of trauma to these sites

Changes in Other Parts of the Body

Face and Trunk Accompanying the changes in the extremities may be involvement of the face and torso As the pathologic process advances in the face it produces the typical masklike facies devoid of wrinkles and furrows with thinning and puckering of the lips and eversion of the lower lip First the patient will notice a tightening of the skin and later there will be difficulty in opening the mouth fully The skin of the chest and abdomen also becomes thick but generally to a less marked degree than elsewhere

Gastrointestinal Tract Although the entire gastrointestinal tract can be the site of scleroderma[illegible] frequent location is the esophagus Symp[illegible] generally appear after scleroderma of the [illegible] common complaints are dysphagia and less frequently substernal burning which occurs about an hour or so after meals especially if the patient lies down at that time Difficulty in swallowing due to esophageal pathology must be differentiated from an inability to get the food off the back of the tongue because of fixation of the oral structures by the sclerodermatous process in these sites The mechanisms responsible for the esophageal symptoms may be stenosis of the lower part of the esophagus esophageal dilatation with atony of the intrinsic musculature spasm at the cardia with obstruction and a shortened esophagus with hiatus hernia The type of change can be determined by x ray and endoscopic examination although it must be pointed out that the latter procedure is not without danger In general esophageal disturbances occur much more often in cases of acrosclerosis than in those of generalized or diffuse scleroderma [0]

Patchy sclerodermatous changes in other parts of the gastrointestinal tract may result in the lack of peristalsis and stasis in both the small and large bowel with narrowing of the lumen X ray examination may reveal these changes as well as rigidity and the appearance of sacculation in both sites but more often in the large bowel

Heart Involvement of this organ may also be present in scleroderma although this usually occurs late in the disease Its presence may be associated with the typical signs and symptoms of congestive heart failure The x ray almost invariably shows moderate to marked enlargement the changes resembling a myxedema heart or pericardial effusion The electrocardiogram generally demonstrates nonspecific signs of myocardial damage

Lungs Some of the findings in scleroderma attributed to cardiac impairment may instead be due to abnormalities in the lungs The hyaline fibrotic changes in the interstitium of the pulmonary parenchyma may lead to the dissolution of the alveolar walls, with the formation of cysts, or to the thickening of these structures, with gradual reduction in the size of the alveoli Bronchiectasis may also develop If the pulmonary vessels are involved, right heart failure and pulmonary hypertension may follow

Treatment

Treatment of scleroderma is, for the most part associated with little hope of permanent improvement If begun early, before widespread irreversible changes have occurred in the bone and soft tissues, therapy may delay the ultimate disability An attempt to increase cutaneous blood flow by removal of vasomotor tonus as through sympathectomy, has been reported as exerting an amelioratory influence on the disease[7] but it is questionable as to whether such an approach will reduce the mechanical blocking of the small vessels by the pathologic process Local application of Mecholyl and histamine by ion transfer (Chap XXV) has also been considered to produce a definite improvement in the condition Since there are very few other procedures which have any effect at all on the pathologic process, such a measure is certainly worthy of a clinical trial

Recently cortisone has been reported to have a definite effect on the clinical appearance of scleroderma and in the pathologic changes as observed in serial skin biopsies The epidermis may become more pliable and softer, with resulting increased mobility of the joints, especially in the fingers However one can not expect restitution to normal Histologically there is a loosening and thinning of the initially thickened and swollen collagen bundles The latter become less closely packed and resume their wavy arrangement Unfortunately the clinical and histologic changes are temporary and there is regression to the previous state soon after the medication is discontinued[27] When the abnormalities in the skin are also associated with a similar type of change in the esophagus causing difficulty in swallowing then the use of cortisone for an indefinite period may be warranted Nevertheless it is necessary to point out that if the recent suggestive evidence of the production of uremia under such circumstances is confirmed this would result in discarding the drug as a therapeutic tool in scleroderma

In addition to medical and surgical attempts to control the condition the patient should be instructed in the local care of the involved extremities Precautions must be taken to prevent trauma to the tips of the fingers since ulcerations may follow such minor injuries as a pin prick Work that is associated with industrial hazards to the extremities should be discouraged The patient should avoid washing his hands in cold water and using strong soaps Exposure to cold should also be reduced to a minimum and the extremities should at all times be well protected when in a cold environment A warm dry climate is preferred Intensive physical therapy may help prevent ankylosis and stiffening of the fingers Active and passive movements massage and whirlpool baths are indicated but such a program must be continued for the rest of the patient s life

Prognosis

The outlook for recovery from scleroderma is dim since the course of the disease is either rapidly or slowly progressive All that can be expected from therapy is a delay in the appearance of ankylosis and the formation of a useless hand Although ulcer formation and gangrene of the fingertips are always a potential hazard they do not contribute directly to the mortality associated with the disease Therefore the patient in whom the sclerodermatous changes are limited to the skin may continue to live for many years as a partial invalid

However when changes are also present in the gastrointestinal tract the heart lungs and other vital organs these may ultimately be responsible for a fatal outcome Usually the prognosis of acrosclerosis is more favorable than that of diffuse scleroderma except when esophageal difficulties appear in the former

POLYARTERITIS (PERIARTERITIS PANARTERITIS) NODOSA

General Considerations

Polyarteritis nodosa is a widespread disease of the vascular system particularly of medium-sized arteries It involves various organs or sites of the body and produces pathologic changes in the function of the affected structures The role that the abnormalities in the extremities play in the clinical picture is of minor importance

Incidence The disorder is somewhat more common in males in the fourth and fifth decades However it may develop at any time from infancy to old age Although it is considered to be a relatively *rare illness* it is possible that the paucity of cases in the literature up to recently has been due to failure to recognize the presence of the entity With the existing clearer understanding of the pathologic and clinical features of the disease an antemortem diagnosis is not too difficult to make

Etiology Many causative agents have been suggested in polyarteritis nodosa but none has been completely accepted The general impression is that although the etiology of this disorder is diverse hypersensitivity plays an important role while psychogenic influences acting through the adrenal cortex may also serve as a contributing agent Experimentally typical lesions have been produced by the injection of numerous antigens into sensitive animals Clinically correlation has been noted between polyarteritis nodosa and allergic phenomena of various types Another possibility is that there is a hypersensitivity angiitis which resembles but is not identical with polyarteritis nodosa [2] On such a basis the widespread use of sulfa drugs and other medications which produce sensitization phenomena may be responsible for the recent increased incidence of cases diagnosed as polyarteritis nodosa

Pathology As a result of the widespread involvement of the arterial tree in polyarteritis nodosa almost all tissues and organs may be affected to varying degrees The ones most often demonstrating pathologic changes are in order of frequency the kidneys the heart the liver the spleen the mesentery the peripheral nerves the skin and the brain [17] On gross examination hemorrhage thrombosis

infarction and aneurysmal formations may be noted Infarcts may be multiple and small, while hemorrhages may be minute in the form of petechiae or extensive, as when an aneurysm ruptures

Microscopically, the predominant alteration is an acute arteritis Degeneration of the media and proliferation of the intima may lead to partial or total occlusion of the lumen, followed by thrombosis (Fig 25) infarction and eventual fibrosis of the involved organ If necrosis of the wall of the vessel occurs, hemorrhage or small aneurysms may be produced Aggregations of neutrophilic and eosinophilic leukocytes, lymphocytes, plasma cells and histiocytes are also present Since the entire thickness of the vessel wall is affected and not just the adventitia and periarterial



Fig 25 Pathologic changes noted in blood vessel produced by polyarteritis nodosa Almost complete filling of lumen by proliferation of intima and secondary thrombosis

tissue the term polyarteritis nodosa is to be preferred to the more commonly used expression *periarteritis nodosa* *It is of significance that* associated with the acute arteritis reparative processes are simultaneously occurring If the condition continues for any period of time organization may take place with proliferation of connective tissue in and around the involved segments of vessels

Clinical Characteristics

Changes in the Extremities

In the limbs polyarteritis nodosa may manifest itself in the form of atypical cutaneous lesions (neurodermatitis vesicle formation urticaria and chronic dermatitis) and ulceration or other trophic changes due to thrombosis of cutaneous arterioles A nonspecific type of purpura may also be observed Another finding is subcutaneous nodules along the course of main vessels some of which may be

pulsating thus indicating the existence of aneurysmal dilatations of the artery It must be pointed out however that such a change is not as frequent as was once believed and that its presence is not necessary in order to make the diagnosis of polyarteritis nodosa

Aside from involvement of nerves elsewhere (see below) the extremities may demonstrate neurologic changes as part of the clinical picture of polyarteritis nodosa Paresis of the extensor muscles of the wrists and wrist drop patchy impairment of light touch in the palms and fingers transient foot drop and absent vibratory sense perception may be noted as a result of a polyneuritis Numbness and tingling may be associated with such findings

Changes in Other Parts of the Body

Since the arterial system of any organ or group of organs may be simultaneously involved and since different stages of the disorder may be present in the various sites at the same time one can expect a diverse symptomatology Hence no attempt will be made to discuss the systemic findings in detail but instead the characteristic symptoms signs and laboratory alterations will be enumerated

Systemic Responses Although no infectious agent has been established as the cause of polyarteritis nodosa many of the symptoms and signs are similar to those observed in patients with acute bacterial infections A low grade irregular and recurrent fever is almost invariably noted some time in the course of the disease Associated with this are chills prostration and changes in the peripheral blood

Circulatory Disturbances Manifestations resulting from changes in the arterial circulation of an organ or organs are protean and they vary depending on the location of the involved vessels The most striking findings are present in the musculoskeletal system Pain tenderness weakness fibrillation and atrophy of voluntary muscles are characteristic changes These may be associated with stiffness of the joints and generalized joint pains

Less often changes are present in the central nervous system Due to thrombosis aneurysmal dilatation and even rupture of the vessels in the brain convulsions and signs of meningeal irritation hemiplegia and cerebellar involvement may be noted As in the case of the peripheral nerves in the extremities the cranial nerves may be the site of polyneuritis with the production of ptosis of the eyelids, paralysis of the extraocular muscles tinnitus deafness and facial weakness

In view of the frequent finding of pathologic changes in the heart one can understand why dyspnea palpitation and precordial pain with or without effort are usually present in polyarteritis nodosa These symptoms are associated with such signs as tachycardia murmurs edema and nonspecific changes in the electrocardiogram

Abnormalities referable to the gastrointestinal system are also a predominant part of the clinical picture These consist of abdominal pain (which is one of the commonest early complaints) weight loss anorexia vomiting and the more severe consequences of thrombosis of the mesenteric artery with infarction of the bowel The findings may mimic a great number of conditions affecting the gastrointestinal

tract, the localizing signs being related to the specific blood supply to the bowel that has been occluded.

Signs of hepatic enlargement and insufficiency may be present if the pathologic changes occur in the vessels supplying the liver. These may simulate several different disorders of the hepatobiliary tract, such as cholecystitis, common duct stone, or atrophic cirrhosis.

Involvement of the pulmonary arteries will generally produce cough, pain in the chest, and asthmatic attacks. Dyspnea is usually also noted, but this may be the result of an associated cardiac insufficiency. Pleuritis, with effusion secondary to pneumonitis or pulmonary infarction, is not uncommon. Bronchiectasis and atelectasis may be present, due to poor ventilation and an inability to expectorate the bronchial secretions.

Since pathologic changes in the kidneys are very frequent, one can expect to find an increase in blood pressure in polyarteritis nodosa. This occurs as a late manifestation and is frequently indistinguishable clinically from malignant hypertension. Renal insufficiency and even uremia may develop.

Diagnostic Aids

Urinary Changes. Among the pertinent laboratory findings in polyarteritis nodosa are alterations in the urine. These consist of albuminuria, hematuria, and cylindruria. Red blood cell casts, oval fat bodies, fatty and waxy casts, and broad casts may all be noted in a single specimen of urine, a finding which has been given diagnostic significance (*telescoped urine*).[16]

Alterations in the Blood. Changes in the peripheral blood are almost invariably present. Although a leukopenia may be noted, in general the white blood count is increased, sometimes to as high as 50,000/cu. mm. The presence of an eosinophilia is of considerable diagnostic importance, but its absence does not rule out the possibility of polyarteritis nodosa. For it is necessary to point out that such a response may be transient and inconsistent, with the result that a positive finding may be obtained only after numerous blood samples have been studied. *The eosinophiles may be increased to as much as 80 per cent of the total number* of white blood cells in the peripheral blood, although generally the count ranges between 20 and 33 per cent. An increasing eosinophilia can be interpreted as indicating activity of the disease. The changes in the white blood cells may be associated with a secondary anemia and an elevated sedimentation rate. A transient positive Wassermann reaction or a similar type of response with other serologic tests for syphilis is also occasionally observed.

Biopsy Studies. It may be necessary in some instances to resort to a biopsy of a subcutaneous nodule—or, in its absence, of skeletal muscle—before the diagnosis of polyarteritis nodosa can be made with certainty. In the case of a muscle biopsy, the specimen of tissue must be taken from a site in which pain and tenderness are experienced; otherwise the histologic sections frequently will demonstrate no pathologic changes, with the result that an incorrect conclusion may be drawn regarding the existence of the disease. It must also be realized that there is always the possibility that the biopsy may contain arteries of skin, subcutaneous fat, and skeletal muscle which have been spared by the pathologic process.

Treatment

Until recently there has been no treatment for polyarteritis nodosa other than symptomatic and supportive measures such as proper diet mechanical support for painful muscles and joints control of congestive heart failure and antibiotics for intercurrent infections However since cortisone and corticotropin (ACTH) have become available several reports have appeared suggesting that these substances may be of value in this condition Their use has produced prompt relief of symptoms and subsidence of the fever in one to three days Although partial relapse may occur when such therapy is terminated improvement follows its resumption It is questionable whether the use of cortisone or ACTH during the critical stage will prevent death

Prognosis

The usual acute case of polyarteritis nodosa goes on to total debility and death in a period of from several weeks to several months [3] However there may be exacerbations and remissions with actual healing in some instances It is possible that the latter outcome may take place in patients in whom progressive changes cease before the vital organs have been extensively involved Furthermore there may be a group of mild cases that are never diagnosed in which normal longevity is not altered Whether the prognosis will be favorably affected by the prolonged administration of cortisone or ACTH can not be stated at present since the period of observation with either drug is still too short

Death in polyarteritis nodosa generally results from congestive heart failure or renal insufficiency Less often it may be due to hemorrhage from rupture of an aneurysm or to necrosis in vital organs

SYSTEMIC (DISSEMINATED) LUPUS ERYTHEMATOSUS

General Considerations

Systemic lupus erythematosus is characterized by widespread collagen tissue damage particularly in the vascular [illegible]
With regard to chronic dis[illegible]
exists as to whether it is purel[illegible] condition[illegible] or a closely related form of systemic lupus erythematosus [28] In any event since it is not associated with any vascular alterations in the extremities it will not be discussed below

Incidence Although it is generally believed that systemic lupus erythematosus is a relatively uncommon disease recent clinical evidence suggests the contrary [8] It is seen predominantly in females especially in the childbearing age In fact it is an infrequent finding after the age of 40 years The condition may affect any race No pertinent information is usually obtained from a review of the past or the family history

Etiology Various factors have been implicated as causes for systemic lupus erythematosus but at present none has been supported by any substantial evidence The theory has been advanced that this disorder is a rheumatoid disease with an

allergic predisposition.[4] However, the fact that there is such a preponderance of the condition in females makes the allergic basis highly improbable. It has also been suggested that all forms of lupus erythematosus have a common pathogenesis based on the response to a number of precipitating causes. From this viewpoint the explanation for the localized type is that the individual with such a lesion maintains a systemic immunity or resistance, while in the case of systemic lupus there is a widespread disturbance of the immune mechanism which is dependent upon the functions of the pituitary adrenal axis.[9]

Several possible precipitating mechanisms have been suggested. There is some clinical evidence to indicate that sensitivity to exposure to sun plays a role in this regard. Whether or not emotional tension can act as an initiating factor is difficult to determine. Furthermore, there appears to be little support for the view that the use of sulfonamides or antibiotics is implicated in such a response.

Pathology. The early histologic changes in systemic lupus erythematosus are swelling of the upper layer of the skin, dilatation of superficial blood vessels and lymphatics in this site, atrophy of the epidermis and liquefaction necrosis of the basal cell layer.[18] A prominent finding is an increase in the number of reticulum fibers. Various degrees of hyperkeratosis are present.

As in the case of other sites, the connective tissue in the blood vessels is also affected. In the most severe phase, the injury of this supporting structure leads to degeneration and even necrosis of the muscular and elastic tissue of the vessel wall. The proliferative phase of the injury to the vascular connective tissue is most apparent in the subendothelial zone of the intima and in the adventitia. This may lead to a bulging of the wall into the lumen, with degeneration of overlying endothelium and resultant plugging of the vessel, a process which can not be distinguished from a thrombus.

Another change consists of the deposit of homogeneous eosinophilic material within the intima, between muscle fibers of the media, or in the adventitia, associated with fibroblastic proliferation. In the case of the intima, this reaction may lead to considerable narrowing of the lumen and, as more and more rings of fibrinoid masses are laid down, eventual complete obstruction of the vessel. Such changes are particularly important in the causation of the pathologic alterations in the central nervous system, intestines, skin, kidneys and ocular fundi.

Clinical Characteristics

The clinical manifestations of systemic lupus erythematosus are variable and unpredictable. Any system in the body may be initially involved and then may heal or show signs of progression, in each stage being represented by a different group of symptoms. The same sequence of events may simultaneously occur in other tissues or it may be delayed for years. This lack of uniform progression in all organs is responsible for the frequent failure to identify the existence of systemic lupus erythematosus early in its inception. The fact that this disorder is subject to numerous remissions and exacerbations also contributes to the diagnostic difficulty.

Vascular Alterations in the Limbs. As in the case of polyarteritis nodosa, the vascular findings in the limbs in systemic lupus erythematosus play only a minor role in the clinical picture. Raynaud's phenomenon may be present, especially in

those patients suffering from involvement of the joints in the extremities In the acute cases there may at times be edema of the legs Although frank gangrene of digits is a rare finding on occasion it may be the most striking part of the clinical manifestations (Fig 76) Even in its presence the main peripheral arteries and the oscillometric readings remain normal The pathologic changes under such circumstances are evidently limited to the small arteries in the digits

Joint Involvement Symptoms referable to the joints are common findings in *systemic lupus erythematosus* the usual complaint being an arthralgic type of pain characterized by mild aching discomfort which passes from joint to joint However there are generally no associated signs of local inflammation such as redness swelling or increased heat and no abnormalities are noted by x ray In



FIG 76 Gangrene of fingers occasionally noted in disseminated lupus erythematosus despite normal pulsations in ulnar and radial arteries

some instances the small and large joints in the limbs may become acutely involved with the local changes resembling those of an acute arthritis Rarely the smaller joints may show changes similar to those of the later stage of rheumatoid arthritis with marked deformity and muscle atrophy and substantiating x ray abnormalities Many patients complain of joint involvement for years prior to the onset of symptoms in other systems

Systemic Responses The clinical course is characterized by a more or less prolonged irregular fever with a tendency to remissions of variable duration At first the fever may be mild but later it becomes septic in type Associated with this response anorexia weight loss malaise and myalgia are common

Cutaneous Lesions In most instances the diagnosis of systemic lupus erythematosus is made chiefly on recognition of the cutaneous lesions The alterations consist of plaques with well defined borders which are indolent and slowly progressive peripherally elevated erythematous and slightly indurated (Fig 77) They are located on the face frequently producing the characteristic butterfly rash a

well as on the scalp, upper part of the chest arms, legs hands and feet Purpuric or petechial lesions are commonly associated with them, being present on the hands and legs A purplish blush is sometimes seen in intensely erythematous areas due to extravasations of red blood cells

Involvement of Vital Organs Invariably several vital organs are affected in systemic lupus erythematosus The one most commonly involved is the kidneys

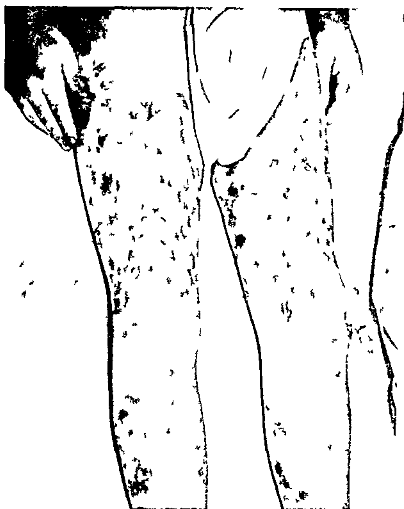


Fig -7 Cutaneous lesions on lower extremities observed in disseminated lupus erythematosus

Despite this, blood pressure is usually not elevated unless severe nephropathy exists kidney function tests may or may not be normal Of interest is the finding of recurrent episodes of elevated blood urea

Gastrointestinal symptoms and signs are prominent These consist of abdominal pain, nausea vomiting and diarrhea Hepatomegaly may also exist No findings of frank peritonitis are generally noted

Cardiac manifestations are also seen Enlargement of the heart is a frequent abnormality while systolic or diastolic murmurs with or without nonbacterial endocarditis are present in more than half the cases Pericardial effusions are not

observed often and friction rubs are rare However, in -5 per cent of the cases pericarditis can be recognized by electrocardiogram or by x ray while necropsy evidence of such an involvement is very common The electrocardiogram in other instances generally demonstrates nonspecific changes An early sign of the presence of the pathologic process in the heart is a tachycardia out of proportion to the fever

Among other findings of importance are generalized lymphadenopathy, mucous membrane lesions facial edema and neurologic or psychiatric manifestations Swelling of the face especially of the lower eyelids is common and usually the degree is a good indication of the severity of the disease With regard to neurologic involvement this may take the form of marked convulsions particularly as a terminal event hemiplegia and toxic psychosis

Pulmonary complications may exist but they are generally of a nonspecific nature and may consist of a diffuse pulmonary infiltration pleurisy with effusion or migratory or recurrent pneumonia Roentgen studies may reveal diffuse perivascular or vascular changes pleuritic effusions and lobar or patchy consolidation The physical findings are usually minimal The changes in the lungs are probably due to general depression of resistance and to alteration of the bronchial or pulmonary structures by the disease process [13]

Diagnostic Aids

Changes in the Blood The peripheral blood frequently shows evidence of a depression of bone marrow activity producing leukopenia thrombocytopenia and anemia Blood cultures are negative The sedimentation rate is generally high and remains so even during remissions An inverted A/G ratio may be present in the serum with a high globulin content (above 2 5 Gm /100 cc) Many cases show a false positive serologic *reaction for* syphilis evidently as the result of changes in the *serum* globulin

Recently a diagnostic test for systemic lupus erythematosus has been described that is also based on some change in the serum gamma globulin It consists of combining normal white blood cells or bone *marrow* in a test tube with plasma from a patient suspected *of* having systemic lupus erythematosus A positive reaction [illegible] ion of the n[illegible] cell) as a [illegible] fragmented material [20] While not always positive in the presence of the disease the test is of considerable importance in the identification of atypical manifestations of systemic lupus erythematosus However it must be pointed out that repeated studies of the blood may be required since the typical cells may be scarce Whether the possibility of a successful attempt is enhanced by the substitution of a bone marrow specimen is problematical

Urinary Findings Because of the consistent pathologic changes in the kidneys abnormal urinary constituents are frequent occurrences in systemic lupus erythematosus The usual findings are albuminuria cylindruria red blood cell casts and microscopic hematuria

Biopsy Studies As a diagnostic procedure histologic examination of a skin biopsy may be of value in less than one fourth of the cases [19] Even when alterations of collagen or fibrinoid changes in superficial vessels are present they are no more

prominent than in many other chronic inflammatory infectious diseases of the skin However, biopsy of an active untreated lesion may reveal dilatation of capillaries and edema of the walls of arterioles and venules, which findings are considered of diagnostic importance

Treatment

Attempts to obtain symptomatic relief form one phase of treatment in systemic lupus erythematosus This involves emphasis on bed rest avoidance of exposure to sunlight and of intercurrent infections and attempts to minimize the systemic complications In the more chronic type a course of bismuth and quinine may be tried as well as the administration of the salts of pantothenic acid or of paramino benzoic acid The cautious use of small and frequent transfusions should be at tempted although it is important to stress the fact that patients who have severe lupus erythematosus are prone to hemoagglutinins or may have severe reactions to whole blood

Recent studies indicate that even the acute stage of the disease can be controlled with adequate doses of cortisone and corticotropin [4, 11, 1] Cortisone administered *orally or intramuscularly in large enough amounts may produce a more rapid* clinical response than comparable quantities of corticotropin On the other hand the latter is preferable in the patient with a stormy course since it prevents severe relapses and slows their onset, thus permitting their detection before the condition of the patient deteriorates into an acute lupus crisis [11] During the acute stage large amounts of either drug should be given at short intervals while in a relapse a daily dose of 200 mg should be sufficient Later the dosage is gradually reduced, but it is inadvisable to discontinue the drugs entirely [11]

There is little question that cortisone or corticotropin is worthy of a trial in the presence of the acute febrile episodes since either may be effective in carrying the patient over a critical period and hence be life saving Frequently such a regimen will produce rapid control of the fever arthralgia tachycardia and the general *symptoms of lupus erythematosus Pleural and pericardial effusions* have also been reported to be promptly reabsorbed

It is necessary to point out however that cortisone or corticotropin will produce a therapeutic response in only certain cases of systemic lupus erythematosus Individuals with a significant degree of renal impairment may show little effect or may even develop *evidences of progressive renal insufficiency during treatment* The changes in the kidney may result from destructive alterations in the structure of the vessels in this organ produced by the drug Because of the possibility of such an untoward effect cortisone or corticotropin should be administered with great caution in the presence of clinical kidney damage

Other possible complications from the use of these drugs are psychosis and con vulsions Since such findings are also common manifestations of lupus at times it may be difficult to differentiate between the two etiologies However convulsions caused by cortisone or corticotropin do not usually occur during the early treat ment phase or before a marked Cushing s state has appeared If the patient has had a recent exacerbation of the disease is febrile has a positive tourniquet test *(Rumpel Leede test)* and shows no evidence of a recent weight gain then the

response is most likely due to the disease itself[3] Another condition for which one should be on guard is the appearance of an infectious process since this requires concomitant intensive antibiotic therapy

PROGNOSIS

It has generally been believed that in the untreated acute type of systemic lupus erythematosus there is no hope of recovery while in the subacute type the mortality rate is about 50 per cent Bronchopneumonia is the usual immediate cause of death although congestive heart failure may be a contributing factor in some cases Spontaneous remissions occur in about [illegible]0 per cent of untreated patients Since the advent of cortisone and corticotropin however the prognosis has been altered somewhat Whether these drugs will produce permanent improvement and prolong life expectancy can not be stated at this time Still there appears to be good evidence that with adequate early therapy, many of the abnormal manifestations can be controlled provided the medication is begun before irreversible damage has occurred[3]

DIFFERENTIAL DIAGNOSIS OF COLLAGEN DISORDERS

Because of the widespread distribution of connective tissue in the body and because of its involvement in collagen disorders the clinical manifestations of the latter diseases may closely simulate each other and even be indistinguishable It is therefore necessary to discuss the pertinent findings of each in the form of a differential diagnosis

Rheumatic Group of Collagen Disorders Inasmuch as systemic lupus erythematosus polyarteritis nodosa dermatomyositis and scleroderma may be associated with manifestations of joint involvement it is necessary to differentiate them from such entities as rheumatic fever and rheumatoid arthritis Such a step is of the greatest importance since serious harm can be done if for example some of the common forms of treatment of rheumatoid arthritis (ultraviolet irradiation fever therapy) are erroneously [illegible] lupus erythematosus The [illegible] in the latter disorder at [illegible] signs and symptoms are minimal contributes to the diagnostic difficulty Of course if constitutional responses are present associated with findings of visceral and serous membrane involvement then the diagnosis is more apparent In such instances further clinical investigation laboratory studies and muscle biopsy are indicated

Systemic Lupus Erythematosus In this disorder the following distinguishing points are of diagnostic importance erythematous lesions of the skin (frequently producing the butterfly distribution on the face) constitutional responses (including cachexia fever and weight loss) arthralgia urinary findings suppression of blood forming elements (resulting in leukopenia anemia and thrombocytopenia) effusion into pericardial pleural and peritoneal cavities nonbacterial endocarditis hyperglobulinemia adenopathy negative blood cultures and the preponderance of involvement in females The presence of L E cells in the plasma marrow

prominent than in many other chronic inflammatory infectious diseases of the skin. However, biopsy of an active untreated lesion may reveal dilatation of capillaries and edema of the walls of arterioles and venules, which findings are considered of diagnostic importance.

Treatment

Attempts to obtain symptomatic relief form one phase of treatment in systemic lupus erythematosus. This involves emphasis on bed rest, avoidance of exposure to sunlight and of intercurrent infections, and attempts to minimize the systemic complications. In the more chronic type, a course of bismuth and quinine may be tried, as well as the administration of the salts of pantothenic acid or of paraminobenzoic acid. The cautious use of small and frequent transfusions should be attempted, although it is important to stress the fact that patients who have severe lupus erythematosus are prone to hemoagglutinins or may have severe reactions to whole blood.

Recent studies indicate that even the acute stage of the disease can be controlled with adequate doses of cortisone and corticotropin.[4, 11, 1] Cortisone administered orally or intramuscularly in large enough amounts may produce a more rapid clinical response than comparable quantities of corticotropin. On the other hand, the latter is preferable in the patient with a stormy course, since it prevents severe relapses and slows their onset, thus permitting their detection before the condition of the patient deteriorates into an acute lupus crisis.[11] During the acute stage, large *amounts of either drug should be given at short intervals, while in a relapse a daily* dose of 200 mg should be sufficient. Later the dosage is gradually reduced, but it is inadvisable to discontinue the drugs entirely.[11]

There is little question that cortisone or corticotropin is worthy of a trial in the presence of the acute febrile episodes, since either may be effective in carrying the patient over a critical period and hence be life saving. Frequently such a regimen will produce rapid control of the fever, arthralgia, tachycardia, and the general symptoms of lupus erythematosus. Pleural and pericardial effusions have also been reported to be promptly reabsorbed.

It is necessary to point out, however, that cortisone or corticotropin will produce a therapeutic response in only certain cases of systemic lupus erythematosus. Individuals with a significant degree of renal impairment may show little effect or may even develop evidences of progressive renal insufficiency during treatment. The changes in the kidney may result from destructive alterations in the structure of the vessels in this organ produced by the drug. Because of the possibility of such an untoward effect, cortisone or corticotropin should be administered with great caution in the presence of clinical kidney damage.

Other possible complications from the use of these drugs are psychosis and convulsions. Since such findings are also common manifestations of lupus, at times it may be difficult to differentiate between the two etiologies. However, convulsions caused by cortisone or corticotropin do not usually occur during the early treatment phase or before a marked Cushing's state has appeared. If the patient has had a recent exacerbation of the disease, is febrile, has a positive tourniquet test (*Rumpel Leede test*), and shows no evidence of a recent weight gain, then the

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preparation is of the greatest import, while muscle biopsy may or may not be of value

Scleroderma In this condition, the prominent findings, at least initially are in the form of alterations in the consistency of the skin Later the changes in the esophagus heart, and other organs may appear Biopsy studies may give pertinent information while changes in the blood are of no diagnostic advantage Since Raynaud s phenomenon is associated with scleroderma it is necessary to differentiate the latter from Raynaud s disease This subject has already been discussed in *Differential Diagnosis* Chapter VIII

Generalized Scleredema Among the less common of the collagen diseases which mimic scleroderma is generalized scleredema This is a benign disorder affecting the deeper portions of the skin and subcutaneous tissues of the body but sparing the epidermis and the muscles[16] It may follow an infectious disease such as tonsillitis influenza, or pharyngitis Typically there is swelling in the nape of the neck which then spreads to the face thorax and shoulders In contrast with scleroderma the hands and feet are not involved in the process Associated with the onset of the edema the patient complains of stiffening of the skin of the involved structures and pain on movement The skin has a pliable waxy feel and is pale Of further importance in regard to differential diagnosis is the absence of pigmentation calcinosis atrophy of muscle, and Raynaud s syndrome in scleredema, as compared with scleroderma in which all these abnormalities may be noted

Dermatomyositis This disorder can be different from scleredema and scleroderma since it is usually progressive and more prostrating An important part of the clinical picture is the erythematous skin lesions which are not present in the other two entities Weakness, muscle pain atrophy and fever are generally prominent findings Biopsy studies may be of great value (For further discussion see Chap XXI)

Polyarteritis Nodosa The distinguishing points in this disorder are the following changes in the blood particularly eosinophilia and leukocytosis abnormalities of urinary sediment hypertension, bizarre and transient neurologic abnormalities, gastrointestinal difficulties and systemic responses If the pathologic state has involved the muscles of the extremities biopsy studies are generally diagnostic

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judged either by clinical reports or by personal observation, even though a number of them have little or no physiologic or experimental basis

TREATMENT OF THE PATIENT WITH NO NUTRITIONAL CHANGES

In the case of the patient who has never had any nutritional disturbances—or having had them has fully recovered—the therapeutic program has several purposes One is to increase muscle circulation and thus enhance walking ability, while another is to reduce the irritability of the peripheral nerves so as to control the rest pain due to ischemic neuritis The most important aims however, are to maintain the cutaneous circulation at a maximal capacity and to protect the skin from injury in order to prevent the onset of ulcers or gangrene for the existence of such lesions may eventually lead to amputation of a limb with its associated risk to life This section deals with the various procedures which are considered efficacious in the fulfillment of the above objectives

ABSTINENCE FROM SMOKING

Thromboangiitis Obliterans In the case of thromboangiitis *obliterans*, most clinical studies support the view that aside from the transient vasoconstriction produced by tobacco smoking this habit is also responsible for a definite aggravation of the pathologic process In many instances such a response will eventually lead to the appearance of nutritional disturbances in the form of *ulceration* and gangrene Merely reducing the number of cigarettes used is of no value whatsoever, nor is the substitution of denicotinized brands worthwhile because at present no completely nicotine free tobacco is available The use of tobacco in any other form is equally contra ndicated Furthermore the fact that the patient does not inhale the smoke should not in any way alter the decision that he abstain entirely In some instances exposing him to patients in advanced stages of thromboangiitis obliterans demonstrating gang ene and lo s of limbs may bring about the desired effect However there will always be a number of individuals who will continue smoking regardless of the steps taken to dissuade them

In the case of the patient who is able to abstain from smoking and given no other treatment clinical improvement may occur or at least obvious progression in the di order will not be apparent Rarely is gangrene noted in such an *individual* unless the limb is traumatized Not only is the pathologic process in the arteries slowed but the attacks of superficial migratory thrombophlebitis are *generally* reduced or even eliminated Whenever there is some question concerning the veracity of the patient's statement that he is abstaining some *corroborative* evidence can be obtained by having him weighed routinely If he has stopped *entirely* he will generally gain weight while if he continues to smoke such a change will not be observed

In summary it can be stated that *the clinical* evidence is so clear-cut that despite the absence of unequivocal physiologic *and* pathologic proof the concept should be accepted that *smoking is definitely* d leterious to the patient with thromboangiitis obliterans *and* hence every *effort* should be made to impress him

CHAPTER

XII VASCULAR ENTITIES PRIMARILY AFFECTING THE ARTERIAL TREE (*Continued*)

5 THERAPEUTIC PROCEDURES IN CONDITIONS WITH PERMANENT ARTERIAL IMPAIRMENT

Therapy in occlusive arterial vascular disorders may be divided into two categories general of value in all such conditions and specific of use in only a particular disease To reduce repetition of material to a minimum it has been felt expedient to present the various procedures that fall into the first group in this chapter rather than to duplicate the effort each time the subject arose in regard to the different clinical entities Those measures which are applicable chiefly to only one of these conditions will be found in the section on treatment in the chapter devoted to the specific clinical entity

Since little can be done to produce recanalization of occluded main arteries the aim of most therapy in chronic obliterative arterial vascular disorders is to establish conditions most conducive *for the ingrowth of a collateral circulation or for an enlargement of an already existing one* Frequently an increase in local blood flow will occur as a natural consequence of the relative anoxia of tissues All that can be *expected with therapy therefore is an acceleration of this process*

The number of procedures which have been advocated for the development of a collateral circulation are legion and no unanimity exists as to the value of most of them In many instances the original claims of the workers proposing the treatment have not been substantiated in other clinics In view of the fact that several of the therapeutic programs are long term procedures involving almost daily contact between physician and patient the role of psychotherapy in the apparent subjective improvement is difficult to evaluate Another objection is that in most cases specific measures have been combined with the abstinence from smoking and the alteration in the clinical course has been attributed to the treatment alone Obviously in the case of thromboangiitis obliterans such an assumption is open to criticism (see below) With certain reservations still in mind therefore the discussion below will deal with those procedures which show some promise as

In this manner although taking a longer time he will be able to cover a much greater distance before experiencing pain The majority of patients have learned to protect themselves from the curious stares of people by window shopping if this subterfuge is available so as to acquire the necessary period of rest without becoming conspicuous Many use canes in order to reduce the weight placed on the involved extremity and thus are able to increase their claudication distance Others have found that if they walk stiff legged without bending their knees or using the calf muscles to any degree the onset of pain is delayed

All the above attempts should be encouraged since a life of physical inactivity generally leads to disuse atrophy of the muscles of the lower extremities with further impairment of walking as well as mental deterioration and the adoption of the role of an incurable invalid Such an attitude is entirely unwarranted and precautions should be taken at all times to prevent it It must be stressed that intermittent claudication produces no serious consequences other than acting as a deterrent to normal physical activity (For further discussion see *Intermittent Claudication* Chap I for physiologic basis see *Intermittent Claudication* Chap XXVIII)

LOCAL CARE OF THE EXTREMITIES

Proper local care of the extremities is a very important aim of the therapeutic program in any type of occlusive arterial vascular disorder Since this part of the regimen is chiefly the responsibility of the patient it is the duty of the physician to explain in detail the reasons for the various measures and the possible serious consequences of neglecting them A printed or mimeographed list of directions (Table 15) may facilitate care and help the patient remember his role in the problem

Local Hygiene and Protection of Feet The feet should be washed daily in lukewarm water and soap and thoroughly dried especially between the toes since these sites are very susceptible to fungus infections Olive oil or some type of hand lotion containing a lanolin base should then be rubbed into the skin of the feet particularly the heel to prevent excessive dryness for otherwise cracking and fissuring may occur Such lesions may become infected and lead to the production of rapidly spreading and painful ulcers

In the winter months all efforts should be made to [illegible] ities warm In [illegible] full length wo[illegible] col[illegible] body from [illegible] vasoconstriction that would ordinarily occur in the vessels of the extremities with such a *stimulus* In an attempt to minimize this factor the patient should expose himself as little as possible to a cold environment and if at all practicable he should move to a *part of the* country where the winters are mild Swimming in the ocean or in pools is likewise contraindicated because of both the local and the reflex vasoconstricting effect of the cold water

At all times attempts should be made to avoid injury to the involved extremities This factor should be considered in advising the patient in his daily program of physical activity particularly in the type of job for which he is fitted With regard

with the great importance of abstaining from this habit (For physiologic reactions to smoking see *Tobacco*, Chap XXX)

Arteriosclerosis Obliterans Whether or not tobacco smoking has a detrimental effect on the patient with arteriosclerosis obliterans who is free of ulcers or gangrene is not known with as much certainty as in the case of thromboangiitis obliterans Nevertheless it is still advisable for him to abstain on general principles In this manner, a potent vasoconstricting stimulus is removed, and as a consequence, the blood supply will be less hampered, thus resulting in increased nourishment to the tissues It is of interest that many individuals with arteriosclerosis obliterans do not smoke at all while in those who do, generally there is not the marked craving for the habit that is frequently observed in patients with thromboangiitis obliterans

Other Occlusive Arterial Vascular Disorders In the case of the patient suffering from arterial impairment following occlusion of a main artery by an embolus or a thrombus or after ligation of the vessel because of injury, abstinence from smoking is also indicated, at least during the acute stage of the disorder Since initially the cutaneous blood flow is precarious elimination of the vasoconstricting effect of smoking helps prevent the occurrence of nutritional disturbances However, later, this factor does not play as significant a role inasmuch as there is normally no tendency to progression of the occlusive vascular disorder in the remaining patent vessels once the main channel has been rendered functionless The only exception to this is when thrombosis occurs in a limb in which pathologic changes exist in other arteries besides the completely occluded one

Physical Activity

Optimal Amount of Exercise The question of how much exercise should be indulged in by the patient suffering from a chronic occlusive vascular disease but still free of trophic disturbances has not been fully answered Some workers believe that intermittent claudication is a warning signal in the same sense that angina pectoris is in coronary artery disease From this viewpoint it would be advisable for the individual to learn the range of effort that is possible without producing symptoms and always stay within it However, there are others of the opinion that graded exercise should be instituted in the hope that the load placed on the vascular system locally will act as a stimulus for the further growth of collateral vessels Certainly the danger attached to the use of such a program for the patient with angina pectoris does not apply in the case of the individual with intermittent claudication If carefully controlled this type of regimen may eventually cause improvement in the ability to walk The patient should be advised to stop exercising with the onset of pain for otherwise it may not immediately disappear during the subsequent period of rest It is even conceivable that if the work load were continued for some time after the appearance of symptoms irreversible changes might occur in the involved muscles

Means of Minimizing the Disability If the patient finds that he is unable to carry out his daily chores without great inconvenience because of having to stop frequently, he should learn to make certain simple readjustments to his disability The most efficacious one is for him to reduce his usual pace considerably

In this manner although taking a longer time he will be able to cover a much greater distance before experiencing pain The majority of patients have learned to protect themselves from the curious stares of people by window shopping if this subterfuge is available so as to acquire the necessary period of rest without becoming conspicuous Many use canes *in order* to reduce the weight placed on the involved extremity and thus are able to increase their claudication distance Others have found that if they walk stiff legged without bending their knees or using the calf muscles to any degree the onset of pain is delayed

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[illegible] warm [illegible] patient wear woolen socks and full length woolen drawers It is also necessary for him to protect the rest of his body from cold in order to reduce reflex vasoconstriction that would ordinarily occur in the vessels of the extremities with such a stimulus In an attempt to minimize this factor the patient should expose himself as little as possible to a cold environment and if at all practicable he should move to a part of the country where the winters are mild Swimming in the ocean or in pools is likewise contraindicated because of both the local and the reflex vasoconstricting effect of the cold water

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to footwear, shoes should be well constructed and of the proper size to prevent the formation of blisters. It may be advisable to place some type of metal covering on the tip of the shoe so as to protect the toes from possible trauma. Special precautions should be taken in trimming the toe nails; they should be cut not too closely and straight across rather than into the angles. If they are hard and brittle, they should receive a preliminary softening by immersion in lukewarm water or oil.

Treatment of Local Nonvascular Lesions. Ingrowing toe nails, corns, callouses and bunions should never be treated by the patient but should be seen by a physician or chiropodist who is acquainted with the fact that a significantly reduced local blood flow exists. An improper approach to such conditions may frequently lead to gangrene. Slight abrasions, blisters or burns should receive especial consideration. The use of the ordinary type of antiseptic, like tincture of iodine or Mercurochrome on minor skin infections is contraindicated because of the possibility of a nonhealing ulcer forming in the partially devitalized tissues. The patient should also be warned against the use of any type of corn plaster applied to a corn or bunion since such a step may initiate a nutritional disturbance. Instead, attempts should be made to remove or minimize the cause of the lesion by using loose fitting footwear, cutting out portions of the shoe which are contributing to the difficulty or attaching nonmedicated felt rings to the skin surrounding the corn, to reduce the pressure on the vulnerable site.

Inasmuch as a fungus infection may initiate the formation of an ulcer or even gangrene, it is essential to prevent its appearance or if already present, to take steps to eradicate it. The patient should be warned to wear wooden shower clogs in public showers, hotel rooms, and gymnasiums. In the treatment of the condition, the procedures utilized should not be strong enough to irritate the skin. The type of therapy depends upon whether or not secondary infection exists and also upon the severity of the epidermatophytosis. In the presence of acute inflammation with lymphangitis, the patient should be at complete bed rest with the involved toes separated using halves of small corks. No ointments should be used but instead various types of soaks are indicated. Among these are solutions of potassium permanganate, first 1:8000 and later 1:4000; silver nitrate, 0.1–0.5%; boric acid, 3%, and a combination of copper sulfate and zinc sulfate in a saturated solution of camphor (Alibour solution). Initially, the feet are soaked twice daily for one half hour and then once a day before retiring. A 1% solution of copper sulfate given by ion transfer is also worthwhile. (For method of administration see Chap. XXV.)

At times the acute inflammatory stage is associated with a systemic reaction which may necessitate the use of other therapy to combat the infection. Sulfa medication or one of the newer antibiotics is preferred to parenterally administered penicillin since the latter may be followed either by an id response or by a generalized allergic reaction which may be very difficult to control. If it is essential to administer penicillin, large doses of an antihistaminic drug should be given at the same time. Furthermore, this should be continued for 1 to 2 weeks after the antibiotic is stopped, for otherwise a delayed allergic response which is even more difficult to control, may appear.

Once the inflammation has subsided and signs of cellulitis or lymphangitis are

no longer present therapy for the most part consists of the use of appropriate ointments or powders. First, the crusting should be treated with a 3% Vioform cream. When this stage is controlled, generally what is left is scaling, which represents the usual case of epidermatophytosis. In its treatment the various fungicides are indicated. Among the better of these are a combination of zinc undecylenate, undecylenic acid and talcum (Desenex), 10% undecylenic acid (Timofax), propionates and caprylate compound (Sopronol) and Asterol dihydrochloride (see *Appendix*). An ointment containing one of these substances should be applied to the lesions at night and the powder during the day. Such a program should be continued for at least 4 weeks, until all manifestations of the fungus infection disappear. At the same time all socks previously worn should be boiled and the shoes should be treated with boric acid powder or exposed to the fumes of formaldehyde to remove any fungi that might be present in the lining. If feasible, it is preferable to use new shoes.

The treatment of nails suffering from a fungus infection (onychomycosis, Fig. 1 E, F [p. 26]) consists of clipping, trimming, and then scraping them twice a day with a glass slide or with a curved piece of glass obtained from a broken electric bulb. Subungual hyperkeratosis should be removed, as well as air pockets which are apparent as white spots on the surface of the nail. Immediately after each scraping the nail should be painted with either a 5% solution of thymol in chloroform or tincture of Asterol dihydrochloride. The commonly used solution of ammoniacal silver nitrate is generally found quite ineffective. However, it must be pointed out that onychomycosis may be resistant to most methods of treatment, including the ones enumerated above. If the nail is also loose from its bed, it should be removed by careful trimming to the point of firm adherence.

Dangers Associated with Application of Local Heat. The direct application of dry or moist heat as a therapeutic agent in occlusive arterial vascular disorders is so fraught with danger that it is rarely used. Since the procedure may initiate various types of nutritional disturbances, particularly burns, ulcers and gangrene, the patient should be warned against applying heating pads, hot water bags or a heating cradle to his feet. An electric blanket, on the other hand, does not introduce any element of danger. (For further discussion, see *Exposure to Local Heat*, Chap. XXVIII.)

TREATMENT OF ISCHEMIC NEURITIS

Little advance has been made in the treatment of ischemic neuritis despite its relatively frequent occurrence in such states as arteriosclerosis obliterans, thromboangiitis obliterans and the chronic stage of sudden occlusion of an artery by an embolus. Although generally therapy is not very effective in combatting the shooting pains and paresthesias experienced when the patient prepares for sleep, still it is worthwhile to attempt several of the procedures enumerated below, since in some instances they may be beneficial in reducing the severity of the complaints.

The patient should be given a course of therapy similar to that advocated for peripheral neuritis. This involves the use of vitamin B_{12}* intramuscularly two or three times a week, large doses of thiamine chloride by mouth (200 mg. three or

* Although at first it was believed that doses as large as 1000 μg were necessary, the impression now is that similar results can be obtained with quantities as small as 50 or 60 μg.

Table 15 General Directions for Home Care of the Feet

1	Wash feet each night with face soap and warm water
2	Dry feet with a clean soft rag *without* rubbing the skin Dry carefully between the toes
3	Always keep your feet warm Use woolen socks or wool-lined shoes in the winter and white cotton socks in warm weather Use a clean pair of socks each day
4	Use loose-fitting bed socks
5	Never apply hot water bottles electric pad or any other form of mechanical heating device to your extremities
6	Wear properly fitting shoes and be particularly careful that they are not too tight Use shoes made of soft leather
7	Cut your toenails in a very good light and only after your feet have been soaked in warm water and cleansed thoroughly Cut the toenails straight across Do not cut down in the corners of the nails If your feet are taken care of by a chiropodist be sure to tell him about your difficulties
8	Do not cut your corns or callouses Never use corn plasters or corn medicine Instead take pressure of shoe off corns bunions or callouses using pads or larger shoes
9	Do not wear circular garters
10	Do not use strong antiseptic drugs on your feet particularly tincture of iodine Lysol or carbolic acid
11	Seek medical care at the first signs of a blister infection of the toes in-growing toenails or trouble with bunions corns or callouses
12	Do not use tobacco in any form
13	Have some member of your family examine your feet at least once a week for blisters sores or other wounds
14	Avoid getting athlete s foot If present be very careful how you treat it Seek your doctor s advice on the matter

four times a day) and intramuscular injections of crude liver extract 1 cc two or three times a week Recently an extract of livers from pregnant cattle (Biohepulin) has been utilized with apparently good results in peripheral neuritis[6, 16] and for this reason it is worthy of a clinical trial in ischemic neuritis also The dose is 5 cc intramuscularly daily for at least ten injections All these steps should be under taken as a long range program since improvement if it occurs can not be expected for several months While the therapeutic program is being carried out vibratory sense perception and pin prick sensation should be tested at intervals of several weeks in order to ascertain whether or not any change is taking place A reduction in the severity of the symptoms experienced by the patient is also of importance

Several other steps should be carried out in conjunction with the above measures The head of the bed should be raised 15 to 20 cm (6 to 8 inches) in order to increase arterial blood flow to the lower extremities during sleep However at the first signs of swelling of the feet the procedure should be discontinued Since

the symptoms at night may be accentuated by the coldness of the feet and by the subjective sense of coldness it is advisable for the patient to wear woolen socks and use an electric blanket when these complaints are present Not infrequently the neuritic symptoms may also then become less annoying

SYMPATHECTOMY

The basis for sympathectomy in the patient with a chronic occlusive arterial vascular disorder but without nutritional disturbances has not been adequately established Examination of the literature on this point reveals conflicting reports in part due to the widespread and at times injudicious use of this procedure

Intermittent Claudication If one is impressed by the data supporting the view that sympathetic innervation of muscle blood vessels is negligible (p 441), then it follows that sympathetic denervation should have little if any effect on increasing muscle blood flow Since intermittent claudication implies an inadequate muscle circulation during periods of work, no advantage should be expected from sympathectomy in reducing or eliminating this symptom in such disorders as thromboangiitis obliterans and arteriosclerosis obliterans In fact the procedure may theoretically at least even aggravate the condition because of the diversion of blood from the uninfluenced partially occluded muscle vessels into the now more dilated cutaneous arterioles and capillaries in the overlying skin

Although the above view is supported by clinical studies[2, 3] there are other reports in which sympathectomy is still advocated when only intermittent claudication exists It is possible that some of the beneficial effects attributed to the operation in the latter studies may have been due to other factors such as the simultaneous institution of a regimen of abstinence from smoking which is generally insisted upon the psychic effects associated with an operation, and the response of the patient to the interest and solicitous attitude of his doctor It is important to point out that if improvement is noted either it is only temporary or it is first experienced as long as a year or more following the operation at a time when a causal relationship is difficult to establish

It would seem therefore that on the basis of available evidence sympathectomy in patients with thromboangiitis obliterans and arteriosclerosis obliterans is not indicated if the sole complaint is intermittent claudication

Value as a Prophylactic Agent The question arises as to whether sympathectomy acts to prevent the appearance of nutritional disturbances Theoretically there would appear to be some basis for such a view since sympathetic denervation is followed by a definite increase in cutaneous blood flow (p 441) Under such circumstances one would expect the skin of the extremity to be less vulnerable to infection and trauma Still no clear-cut extensive and long range clinical studies exist to indicate that there is a statistically significant reduction in the incidence of trophic changes in sympathectomized extremities as compared with a comparable group of nonoperated patients In fact in most of the papers which deal with this subject control series are lacking One point that does come out of the available evidence is that in thromboangiitis obliterans ulcers and gangrene still form after sympathectomy[11] particularly if smoking is continued[1, 3] In the

case of arteriosclerosis obliterans, the procedure seems to have some protective action in this regard.[1,3]

Therefore, it can be concluded that at present widespread prophylactic use of sympathectomy in patients with chronic occlusive arterial vascular disorders is not warranted. However, in specific instances the measure may be considered for this purpose, as for example, when one limb has already been amputated because of gangrene and the other is involved but not to the extent that nutritional changes have formed.

TREATMENT OF THE PATIENT WITH AN ULCERATIVE OR GANGRENOUS LESION

If, despite the use of the measures already discussed, an ulcer or gangrene occurs, intensive therapy should be instituted at once to limit the spread of the nutritional disturbance and, if possible, to facilitate rapid healing of the involved site. For the most part, the various procedures are similar, regardless of whether the underlying mechanism for the impaired circulation is thromboangiitis obliterans, arteriosclerosis obliterans, or an occluded or surgically ligated main arterial trunk.*

In the final analysis, the results that can be expected from the treatment of nutritional disturbances will depend primarily upon whether the vascular or the infectious component predominates as the etiologic agent. Obviously, if the local blood supply continues to diminish because of the natural or accelerated progression of the occlusive process in the cutaneous vessels, ulceration or gangrene will invariably spread, regardless of the therapy utilized. Under these circumstances, the only means available for the augmentation of the circulation is dilatation of the unaffected collateral system, a response which may at times help preserve the viability of the limb.

In contrast, the control of infection is more readily accomplished. When successful, it will tend to minimize the further destruction of tissues by the inflammatory response and at the same time reduce the likelihood of thrombosis of small arteries in the region of the involved area. Both results contribute to the localization of the nutritional disturbance.

In the case of an ulcerative lesion, infection may or may not play an important role. For example, in the patient with thromboangiitis obliterans, it is generally of minor significance, since the lesion in such an individual appears to be fairly resistant to this complication. On the other hand, an ulcer in an individual who is suffering from diabetes mellitus as well as arteriosclerosis obliterans will almost invariably be secondarily infected. In the presence of arteriosclerosis obliterans alone, the incidence of this type of response is only somewhat greater than in the case of thromboangiitis obliterans.

In most gangrenous lesions the predominant underlying mechanism is vascular insufficiency, while infection is usually minimal. If the tissues are mummified, as in

* Generally, gangrene or ulceration following frostbite, trench foot, immersion foot, and Raynaud's disease is also treated in the same manner.

dry gangrene saphrophytic bacteria may be present in the interior of the necrotic material but rarely is there spread into the neighboring viable structures At times in the presence of wet gangrene extensive invasion of the inflammatory process into bones and along tissue planes and tendon sheaths may take place (For a discussion of wet and 'dry gangrene see Gangrene Chap VII)

GENERAL SUPPORTIVE MEASURES

In the treatment of trophic changes it is necessary first to improve the general physical condition of the patient through counteracting any anemia supplying a nourishing and high caloric diet if debility is present and providing for adequate amounts of rest and sleep

Control of Pain This is a very important part of the therapeutic program and if successful it permits a less hurried and hence more effective *approach to the* problem of healing of ulcers On the other hand symptoms which *do* not respond to any of the available methods may necessitate amputation of a limb at a time when this step would not be warranted solely on the basis of the degree of involvement of the tissues

Since it is imperative that the patient *receive* a proper amount of rest agents which control the *pain* should be given freely at least for short periods of time Morphine *sulfate* 16 mg (¼ gr) intramuscularly and meperidine (Demerol) hydrochloride up to 100 mg may be effective in this regard An intravenous injection of 1000 cc of a 0 1% solution of procaine hydrochloride administered over a period *of one* to one and one *half hours* and repeated daily may also be useful Sympathetic blocking drugs *and* sympathectomy by increasing blood flow are of value *in reducing the irritability* of the ischemic nerve endings and hence the pain Obviously this is an approach to the problem that is preferable to the use of narcotics

Crushing of sensory nerves has a limited application in the treatment of pain It should be utilized only when all other means have been tried and f...
tive and the alte...
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pain ... the change in
the ... following nerve crushing is spectacular Furthermore the patient will now allow intensive local *treatment* to the lesion whereas previously the mere contact with a light bandage would have been sufficient to initiate severe symptoms The fact that the procedure also interrupts vasoconstrictor impulses by destroying the sympathetic fibers in the somatic nerves may be responsible for part of the therapeutic result since there is a consequent increase in local circulation Another possibility is that afferent impulses traveling over sympathetic pathways are likewise interrupted

The procedure has much less clinical application in arterio clerosis obliterans First the problem of severe pain that can not be controlled by medical therapy is by no means as common as in thromboangiitis obliterans Second in the former condition wallerian degeneration and fibrosis of the terminal portions of the peripheral nerves are fairly common histologic findings and therefore crushing of these structures cephalad to the involvement may be ineffective in reducing or

eliminating the pain. It is possible that the continuous irritation of the endings by the pathologic process causes a build up to the point that some conduction of pain impulses occurs, either through the crushed segment of nerve or over new pathways.

There are certain disadvantages and dangers associated with nerve crushing. The chief objection is that the foot remains anesthetic for 3 to 6 months or longer until regeneration of the nerves occurs. In this interval the patient must be careful to wear well fitting shoes and not to apply heat to the limb, for otherwise new and serious nutritional disturbances may result. Another untoward effect is the resulting paralysis of the intrinsic muscles of the foot, which, however, does not interfere to any great extent with walking. A possibility which may have grave consequences is infection following nerve crushing. This is particularly so in the case of the patient with arteriosclerosis obliterans who also has diabetes mellitus. Obviously such a situation in the face of an impaired cutaneous circulation at the level of the operative sites may aggravate rather than help the condition. It is therefore necessary to keep traumatization of tissues to a minimum and to pay scrupulous attention to asepsis at the time of operation and subsequently. Even with such precautions, an indolent nonhealing ulcer may still form.

It would seem, therefore, that in the treatment of pain associated with nutritional disturbances all available means should be utilized, including nerve crushing, although the latter is applicable only when less heroic measures have failed. If successful in this aim, amputation can then be delayed perhaps indefinitely.

Bed Rest. Physical activity should be sharply curtailed in the presence of ulceration or gangrene, since walking may facilitate spread of any existing infection and extend the size of the involved lesion. Rest is a very important factor in the healing of trophic disturbances, and hence the patient should be kept in bed for as long as practicable. If it is necessary for him to walk, this should be done with the aid of crutches so as to avoid weight bearing. Institutional care is preferred to bed rest at home, inasmuch as conditions can more readily be controlled. However, since the period of treatment is generally prolonged, the financial outlay associated with hospital care frequently makes this inadvisable.

Position of Limb in Bed. While the patient is in bed, the involved extremity should be lying in a horizontal position and not raised on a pillow or placed in dependency. Elevation causes a decrease in arterial blood flow, since hydrostatic pressure is now working against the small blood pressure that exists in the nearly occluded arteries. As a result, anoxia is enhanced. Frequently patients with extensive ulcers are made aware of this situation by the fact that their pain is markedly exaggerated when the observer raises the extremity in the course of the vascular examination. On the other hand, there are occasional individuals with trophic disturbances who actually obtain relief when this is done. Such a paradox is difficult to explain, unless one assumes that in the horizontal position the irritated nerves are being subjected to pressure which is reduced when the leg is raised, since in the latter position pooled blood and lymph, previously distending the tissues, are drained rapidly out of the extremity by gravity.

Most patients find that allowing their involved limb to hang freely over the bed or to rest on a chair affords a certain amount of relief from the severe pain. As a

result they will tend to sleep in this position It is true that under these circumstances the movement of blood into the distal portion of the extremity is facilitated by hydrostatic pressure and that local tissue nourishment is temporarily enhanced However if the leg remains in dependency the foot will generally become swollen (Fig 8 p 85) * This type of response will further enhance the anoxia because of the obstructing pressure that the edema fluid exerts on the thin walled partly filled cutaneous capillaries It therefore becomes necessary to break the vicious cycle so as to eliminate the edema for if prolonged it may contribute to the extension of the nutritional disturbance The patient should be strongly urged to keep his feet flat in bed while the resulting increase in pain will have to be controlled by narcotics or the use of procaine intravenously (see above) In the event that he is unable to exert sufficient will power to follow these directions it may be necessary to give him a general anesthetic in the form of barbiturates administered intravenously and elevate the extremity to remove as much of the fluid as possible This is done in the hope that with the elimination of the swelling there will occur enough improvement in local circulation to reduce the anoxia of nerves and consequently the pain As a result the patient may now be in a more cooperative mood with regard to maintaining his limb in the horizontal position

MEANS FOR IMPROVING CUTANEOUS CIRCULATION

Although as already mentioned very little can be done to retard the rate of progress of the occlusive process in the arterial tree still an effort should be made to maintain the cutaneous circulation at a maximal state of dilatation This can be attempted through the use of certain drugs and procedures which either remove vasomotor tonus transiently or permanently or augment the blood supply of the skin through other means

Medical Therapy

Vasodilator and Adrenergic Blocking Drugs In every patient with an ischemic ulcer or gangrene the intensive use of one or several vasodilating drugs is worthy of a clinical trial Among these are orally or intravenously administered nicotinic acid (50-100 mg) oral whisky 2 or 3 times a day and sympathetic blocking agents Of the latter Priscoline has had the widest clinical application It may be given orally (25 mg 3 to 5 times a day) intramuscularly (50–75 mg at 6-hour intervals) or in certain selected cases intra arterially [18] Others which have been used are Hydergine administered orally (0 5 mg sublingual tablets 3 times a day) or intramuscularly (0 3 mg once a day) and oral Dibenzyline (10 mg 3 times a day) Unfortunately with all these medications one can rarely expect the improvement in the nutritional disturbance to be spectacular and in most instances it is minimal or not noted at all (For pharmacologic action of these drugs see Chap XXX)

Indirect Vasodilatation A simple procedure for increasing cutaneous blood flow to the lower extremities is the application of heat to distant portions of the

* For basis for edema see *Pathologic Edema* Chap XXVIII

body, to produce indirect vasodilatation through removal of vasomotor *tonus*. Aside from the measures discussed in Chapter IV, the desired effect can also be accomplished by enclosing the upper extremities, up to the arms, in metal cuffs *composed of protected heating coils*.[4] Since the increased local circulation occurs without any significant rise in tissue metabolism, the treatment can be repeated several times daily. The fact that the vasodilating response is maintained during the entire period of application and for a short time afterward makes the method a valuable adjunct in the control of ulceration and gangrene at a time when sympathectomy is not as yet considered advisable.

Use of Anticoagulants. In some instances, in the presence of impending gangrene, anticoagulants are indicated since they may help prevent the propagation of the thrombotic process into neighboring arteries, thus limiting the area of devitalized tissue. This is especially true if there is a tendency for thrombosis to occur in the arcuate vessels in the foot from which the digital arteries arise. If inflammation and infection are present, the use of anticoagulants may also help to counteract clotting in those vessels traversing the involved tissues.

Use of Mechanical Procedures

In recent years a number of different mechanical devices have appeared on the market which were enthusiastically acclaimed by their originators as being very effective in increasing local blood flow to the extremities. However, these views for the most part have not been substantiated by other workers and as a result several of the methods have been, or should be, discarded as therapeutic aids. *Among those that are still being utilized clinically are postural* exercises, the Sanders oscillating bed, the Pavaex boot, and intermittent venous occlusion.

Postural Exercises (Buerger's Exercises). The procedure of successively placing the lower extremities in various positions has the advantage of requiring no special apparatus or supervision and hence can be carried out by the individual at frequent intervals. It can be utilized both by the ambulatory patient and by the one at complete bed rest. The cycle consists of the following:

The subject lies on his back in bed and maintains the lower extremities at an angle of about 45 degrees for 2 minutes. Then he sits up and allows the limbs to rest in dependency over the edge of the bed for 2–3 minutes. During this time each foot is moved inward and outward, the ankle is moved downward and upward, and the toes are alternately spread and closed. At the end of this period the patient returns to the horizontal position but with the entire body flat in bed. After 2 minutes the cycle is repeated. A treatment consists of 4 or 5 cycles in succession and this is performed 2 to 4 times daily. A worthwhile supplementary step is to wrap the patient in blankets and keep him warm through the use of hot water bags placed around the trunk for about 15 minutes after completing each treatment.

Postural exercises appear to have some place as an adjunct to other therapeutic procedures used in thromboangiitis obliterans and arteriosclerosis obliterans. Although the measure does not affect intermittent claudication to any obvious degree, it may cause temporary alleviation of rest pain associated with ulceration

and gangrene On occasion after prolonged use the relief may persist for some time after treatment is terminated The beneficial effect is considered to be related to an increase in blood flow consequent to the emptying and filling of the vessels by gravity a point which has never been satisfactorily proved

Sanders Oscillating Bed A motorized oscillating bed may be substituted for the postural exercises for the purpose of producing cyclic positional changes[18] It has the principle advantage of emptying the veins in the extremities without any active movement on the part of the subject This is of value in the case of debilitated or weak patients who may find the effort necessary to maintain the extremities elevated for 2 minutes a feat beyond their limited strength The tilting apparatus of the bed is so controlled that the duration of each part of the cycle can be readily altered The procedure is particularly useful for bed patients since the exercise can be carried out continuously during the day and even throughout the night

The therapeutic effects of the oscillating bed are similar to those mentioned for the postural exercises However it is questionable whether the expenditure of a large sum of money for this apparatus is warranted in view of the doubtful physiologic basis for the procedure and also the minor degree of improvement that can be expected

Pavaex Boot This method consists of the alternate application of positive and negative pressure to a limb enclosed in a boot The levels of pressure originally suggested were a positive one of 20 mm Hg for 3 seconds followed by a negative one of 80 mm Hg for 12 seconds[8] These steps have since been modified by other workers The method at one time had wide use and courses of treatment were available in almost all hospitals

The rationale for the use of this type of apparatus is not clear nor has any convincing experimental evidence been presented to support the view that it increases the peripheral circulation in a limb with nonfunctioning blood vessels In the presence of an acute infection associated with ulceration or gangrene the use of the Pavaex boot is dangerous since the repeated application of the positive and negative pressures may cause progression of the process into the lymphatics and surrounding tissues In general then the measure plays little or no role as therapy in chronic occlusive arterial vascular disorders

Intermittent Venous Occlusion This method utilizes a modified blood pressure cuff through which a positive pressure of 30–60 mm Hg is alternately applied to the thigh[5] The usual cycle consists of 1 to 2 minutes on and 2 to 3 minutes off for 15 30 minute periods three times a day However some patients are able to use it during the entire night without it interfering with sleep The height of the pressure is generally maintained below the patient s diastolic blood pressure level (For types of machines see Appendix)

Several [illegible]

ro[illegible]

th[illegible] to the skin of the [illegible] the repeated application of the pressure may produce ridging and irritation of the skin beneath the cuff Second if the latter is placed loosely around the thigh the full effect of the pressure will not be exerted on the tissues of the extremity Finally the apparatus must be routinely inspected

and adjusted, for otherwise the valves may suddenly stop working If this takes place while the cuff is in the inflated position and if the patient is asleep the situation may persist until he awakens in the morning As a result, the extremity will be subjected to prolonged venous congestion, which is not desirable in the presence of an impaired arterial circulation

Again, as in the case of the Pavaex boot, there is no clear-cut evidence to substantiate the view that the intermittent application of a venous occlusive pressure has a beneficial effect on the local circulation *The procedure causes a corresponding* rise in venous pressure in the limb and the trapping of a large quantity of blood in the venous bed but this situation does not result in any vasodilatation when the pressure is released Still there are several clinical reports indicating that the procedure may be of value in occlusive arterial vascular diseases Although it does not appear to increase walking distance in thromboangiitis obliterans or arteriosclerosis obliterans, it may contribute to healing of small well demarcated and chronic ulcers demonstrating a minimum of infection The possibility of spreading the inflammation in a case of this type is very much less than with Pavaex However if an acute inflammation is associated with the nutritional disturbance, the measure is generally contraindicated

In summary it can be stated that there is no objection to a clinical trial with the intermittent venous occlusion apparatus since in most instances it has no untoward reactions if it is carefully controlled In addition it may be psychologically useful since the patient feels that he is receiving some type of treatment

Sympathectomy

While sympathectomy is of little value as therapy in the patient who is free of nutritional disturbances (see above), it appears to have a definite place when such changes are present This is particularly true if the various medical measures have been found to be of no avail either in healing or in preventing extension of the ulcer or gangrene The operation may contribute to a successful outcome after amputation of a gangrenous toe although its efficacy in saving a limb if the process has already extended onto the adjoining portion of the foot is doubtful Furthermore in those instances in which ulcers heal following sympathectomy the possibility still exists for the recurrence of these or for the appearance of similar lesions elsewhere on the extremity In the full evaluation of this procedure it is necessary also to consider its limitations and possible untoward effects These subjects are discussed in *Limitations of operation* and *Complications of* sympathectomy in Chapter XXVII

MEANS FOR COMBATTING LOCAL INFECTION

Since infection lends itself more rapidly to treatment than does an impaired cutaneous circulation all possible means should be utilized in its control However at the outset it must be realized that this aim is accomplished with much more difficulty in the case of the ischemic ulcer than in the nonvascular type of lesion One reason is that the efficacy of the available antibacterial substances is limited by the fact that a potent concentration of drug is difficult to achieve in the involved

ate because of the marked impairment of local circulation Second antibiotics are not effective in the presence of necrotic tissue, which is a frequent finding in ischemic ulcers Nevertheless a clinical trial with such agents is indicated

Local Measures

General Precautions As a general rule in the local treatment of secondary infection associated with a nutritional disturbance care must be exercised at all times to limit the choice of topical medication or other measures to ones which will in no way exert a deleterious effect upon the tissues themselves *Strong antiseptics* are definitely contraindicated because of their destructive action on partially devitalized structures In fact their use may lead to an alarming extension of the ulcerative or gangrenous lesion For similar reasons heat should not be applied to the limb despite the presence of inflammation * It is also advisable not to allow adhesive tape to come in direct contact with the skin since repeated exposure of the same area to this irritant may result in the formation of superficial ulcerations At no time should tight bandages be placed around the foot or leg since they may further reduce the impaired circulation If strips of adhesive tape are used over the dressings care must be taken not to allow any of them to encircle the foot completely unless loosely applied All these warnings are especially timely when it is found necessary to treat an extremity with a nutritional disturbance for a fracture

Local Soaks When large quantities of secretion and pus exist it is necessary to cleanse the wound daily using various bland solutions Lukewarm foot baths containing tincture of green soap are of advantage in washing off the loose necrotic tissue They should be taken in basins sufficiently large to accommodate the extremity without difficulty If the patient is unable to stand the pain which may follow immersion of the involved foot it may be necessary to resort to neomycin soaks or to irrigation of the areas with hydrogen peroxide or sterile saturated boric acid solution using a hand syringe After each treatment close attention must be paid to drying the entire foot carefully particularly between the toes In a diabetic patient since there is a possibility that the skin of the feet may respond poorly to soaking such a procedure should not be carried out over a prolonged period of time unless the tissues can be examined at frequent intervals for signs of maceration and irritation For similar reasons antibiotics in an ointment base are preferred to ones in a watery solution when it is necessary to apply them topically in this type of individual

Removal of Eschar If necrotic tissue partly or completely covers an ulcerative area it is necessary to remove this material before instituting any other therapy Such a step prevents the growth of bacteria and at the same time allows the various topical medications to exert their therapeutic effect directly on the infected viable tissue If the commonly found heavy adherent eschar does not

* On rare occasions when it is felt necessary to raise the temperature around the involved extremity this should be done under careful supervision using a thermostatically controlled heater to produce a uniform and consistent effect At the same time the source of heat should be so protected that there is no possibility of the limb coming into direct contact with it and the environmental temperature should never be allowed to go higher than 35 C (95 F) If these precautions can not be taken it is advisable to discard such a procedure

respond to simple debridement without a general anesthetic then either Azochloramid in oil or a solution of Tryptar or Vandase (p 501) should be tried In the case of Azochloramid the normal skin around the lesion is covered with sterile petrolatum jelly for protection and gauze saturated with the solution is placed over the ulcer itself The area is kept wet by the application of the material to the dressing several times a day, using a sterile medicine dropper After several days of treatment another attempt is made to remove the necrotic tissue If not successful then the same treatment is continued until a clean ulcer base is obtained It is important to point out that none of these irritating substances should be applied beneath an occlusive dressing (see below)

Sensitivity Studies One of the first steps in the treatment of the local infection is to obtain a culture of the bacteria present in the lesion and to determine their sensitivity to the available antibacterial substances For this purpose, it is advisable to remove the debris and discontinue all local treatment The ulcer is cleaned with hydrogen peroxide and covered with a dry sterile dressing for a day or two at the end of which time a smear is made of the secretion that has accumulated in the base of the wound This is then utilized for the growth of a culture and for subsequent sensitivity studies [10] In this manner the indiscriminate and blind use of antibacterial agents is minimized with a consequent financial saving to the patient and a better possibility of controlling the infection

Use of Topical Antibacterial Agents Once information has been obtained regarding the relative effectiveness of the antibacterial agents the appropriate ones should be used both locally and parenterally (see below) Among those which have received extensive clinical trial are bacitracin, neomycin tyrothricin Sulfamylon with streptomycin, Aureomycin and Chloromycetin They are available either in an ointment base or in aqueous solution In order for topical antibacterial therapy to be successful there must—in addition to the removal of necrotic tissue and the use of sensitivity tests—be adequate and constant contact between the site of infection and the drug Recontamination with resistant organisms must be prevented and the antibacterial substances themselves should be well tolerated by the involved tissues and not inhibited in the wound [9]

When the antibacterial agent is administered in an aqueous form the application of an occlusive bandage will reduce the amount of solution necessary to keep the wound wet and continually exposed to a fresh supply of the drug Utilizing careful sterile precautions this is accomplished in the following manner [9] A layer of sterile gauze cut to conform exactly to the outline of the lesion is placed over it, so as to act as a wick to carry the medication into all crevices One or more #8 or 10 French rubber catheters are used to convey the solution to the wound one end remaining in contact with the gauze while the other emerges from the dressing To prevent formation of new ulcerations a protective thickness of petrolatum gauze is inserted beneath each catheter wherever it comes in contact with skin The whole site is covered by a sheet of well lubricated gauze and a bulkier layer of surgical gauze over which a sterile rubber sheeting is placed In this manner the dressing is made waterproof and evaporation of solution is prevented

The occlusive dressing is left in place for 4–6 days [9] Every 4–6 hours during

this period 2-4 cc of the aqueous solution of the antibiotic is injected into the rubber bulb of sterile medicine droppers inserted into the open end of the catheters This is always followed by several cubic centimeters of air to blow the material through Between administrations the medicine droppers are kept covered with sterile gauze If infection has not been controlled after the first application of the dressing re-evaluation through new culture and sensitivity studies is indicated for the flora may have changed and a resistant organism may now predominate Although some wrinkling of surrounding normal skin may be present upon removal of the dressing maceration of tissue rarely occurs[9] However for reasons already mentioned this type of procedure should not be used in the diabetic individual

Treatment of Gangrene When infection is minimal while the predominant change is local death of tissue limited to a toe or toes a conservative attitude should be assumed in the hope that demarcation and spontaneous amputation may take place If the gangrenous material on the involved digit has become loosened or if it is causing pressure on the toes on either side it is advisable to remove it under careful sterile precautions without the use of anesthesia However it is necessary to emphasize the importance of limiting the procedure to segments some distance away from viable tissue Under these circumstances no pain should be experienced and no bleeding should occur The measure if performed properly may expedite healing without encouraging progression of the gangrene The involved region should always be kept covered by sterile bandages and protected from trauma If the process appears stationary and there are no signs of inflammation there is no contraindication to the patient resuming a certain amount of physical activity But it must be realized that such a situation is not entirely free of danger and that the lesion is an excellent site for secondary infection Hence the patient should be kept under close observation so that the beginning of difficulties can be immediately recognized The physician should embark on this type of program with the realization that it will have to be in effect for months before all the necrotic tissue can be expected to slough spontaneously and permit healing of the base of the toe

An alternate method for dealing with gangrene that is limited to the toes is surgical removal of the necrotic material under anesthesia This involves incision through viable tissues with all the potential risk associated with such a step If healing takes place by first intention then the patient is spared a prolonged period of medical therapy However in most instances the operative site slowly covers over so that very little time is actually saved by the procedure Of course if an ulcer subsequently forms in the vicinity of the incision then the treatment becomes even more protracted Finally the operation may result in further destruction of tissue and extension onto the adjoining portion of the foot thus ultimately necessitating amputation of the limb To prevent such a possibility a preliminary lumbar sympathectomy may be worthwhile

Parenteral Administration of Antibacterial Drugs

Besides the topical application of appropriate antibacterial drugs their systemic administration through the usual routes is also of value as a supplementary

respond to simple debridement without a general anesthetic then either Azochloramid in oil or a solution of Tryptar or Varidase (p 501) should be tried In the case of Azochloramid the normal skin around the lesion is covered with sterile petrolatum jelly for protection and gauze saturated with the solution is placed over the ulcer itself The area is kept wet by the application of the material to the dressing several times a day using a sterile medicine dropper After several days of treatment, another attempt is made to remove the necrotic tissue If not successful, then the same treatment is continued until a clean ulcer base is obtained It is important to point out that none of these irritating substances should be applied beneath an occlusive dressing (see below)

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whether they have any therapeutic action on the clean ulcer However they do help protect the delicate newly forming tissues from the irritation of a dry dressing

Factors Affecting Outcome of Therapy

Aside from the natural or accelerated progression of the occlusive change other factors may influence the results of treatment of nutritional disturbances Among these are the spread of the process to underlying bony structures the poor prognosis associated with involvement of certain portions of the extremities and the great financial outlay necessitated by prolonged conservative therapy

Osteomyelitis Whenever an ulcer becomes indolent and resistant to therapy the possibility of the existence of chronic osteomyelitis must be considered If x ray evidence of this state is found there is generally no basis for further medical treatment since this will probably be ineffective Instead the lesion should be debrided under anesthesia and the necrotic bone removed It is important to emphasize the fact that concomitant involvement of bony structures makes the prognosis much graver regardless of the type of treatment

Poor Prognosis Associated with Certain Sites Although with the program outlined in this chapter many of the smaller ulcers will frequently heal their location in certain portions of the foot will reduce this possibility For example a lesion situated close to the margin of a nail responds much more poorly to treatment than one a little distance away This is particularly true in the case of the great toe It may be that the continued irritation of the tissues by the sharp edge of the nail tends to interfere with the healing processes Frequently the removal of the nail has a definitely beneficial effect on the lesion especially when it is found to be loosely attached indicating that it has been involved in the inflammatory process

Healing of ulcers or gangrene in the heel is also protracted or unsuccessful Ordinarily this portion of the foot is covered by several layers of dead epithelium and the tissues underneath have a relatively poor blood supply The fact that the sweat and sebaceous glands are scanty here makes the tissues even more susceptible to cracking and fissuring In the presence of an impaired local circulation this tendency is exaggerated with the result that a large sized ulcer may form rapidly from a minor crack in the skin

A nutritional disturbance of the first and fifth toes is more frequently followed by progression onto the adjoining portion of the foot than in the case of the other digits The fact that the first toe receives its collateral circulation from one side only may be the explanation for its relatively greater vulnerability to ulceration and gangrene and the more rapid spread of the process when once initiated At the same time there is a much larger bulk of tissue involved as compared with the other digits which contributes to a poorer prognosis

Financial Cost of Protracted Therapy Another factor which unfortunately influences the type of therapeutic result is the economic pressure built up by prolonged treatment Generally such a program involves one or more hospitalizations and a large outlay of money The fact that the patient usually can not be gainfully employed during the entire period of observation further contributes to hi financial difficulties As a result the physician may feel compelled to take short

measure In an attempt to build up the concentration of the therapeutic agent in the involved tissues the intra arterial injection of such substances as penicillin has likewise been proposed [19] With this type of procedure dilution of the material is minimal and at the same time the blood pressure forces the drug into the local area supplied by the artery The factor of increased capillary permeability resulting from the inflammatory process permits a greater filtration of the agent locally The technic of intra arterial injection of penicillin is as follows

Vasodilatation of the involved limb is produced by soaking it in warm potassium permanganate solution (1 9000) for 20 minutes Then a blood pressure cuff is placed around the extremity proximal to the infected portion and inflated to a pressure of 80 mm Hg Following this 50 000 units of the drug in 10 cc of saline solution is injected into the main artery of the limb over a period of 10 seconds using a # 20 gauge needle 5 cm (2 inches) long The pressure in the cuff is maintained at the original level for 10 minutes after the termination of the injection The drug may be given once or twice daily in this manner

There are however several objections to the routine use of intra arterial administration of penicillin First the procedure can not always be accomplished readily and it has no clinical application when the femoral artery on the affected side is obliterated Second, there is always the risk of initiating spasm in an already diseased vessel either as a result of the necessarily multiple punctures or through extravasation of the material into the vascular sheath and the surrounding tissues Another possibility to be considered is dislodgment of atheromatous plaques

In summary the intramuscular and oral administration of antibacterial agents although not always controlling the local infection may be of great value in limiting the extent of its spread thus preventing septicemia This is particularly true in the case of the diabetic individual In certain selected cases in which infection plays an important role intra arterial administration of the drug is also useful since it may overcome the difficulties offered by tissue barriers and vascular impairment conditions which reduce the efficacy of all antibacterial agents when given intramuscularly or orally [19]

Means to Facilitate Healing

Once the lesion appears fairly clean and infection is controlled attempts should be directed toward accelerating the healing process In this regard it is advisable to cleanse and dress the site much less frequently for repeated manipulation may cause injury to fine blood vessels and new tissue and inhibit the rate of epithelialization At the same time the use of the ointments should be discontinued since at this stage they too may have the same effect However if secretion increases and signs of infection reappear they should be applied again

Local Stimulating Substances Many drugs have been advocated for the purpose of facilitating the rate of growth of skin and subcutaneous tissues over an ulcer site Among these are chlorophyll ointment (Chloresium ointment) White s A and D ointment (made up primarily of cod liver oil) vitamin A ointment red blood cell powder (Lyocyte powder) and coal tar products (Daxalan ointment) Some of these might be given a clinical trial although it is questionable as to

time the large financial cost and the debilitating effect of a prolonged illness have generally produced a marked lowering of his morale and physical stamina and hence he suffers from a profound sense of discouragement All means must be utilized therefore in the dissipation of such a mental attitude

If the patient persists in his unwillingness to submit to operation the serious consequences that would inevitably follow should be brought graphically to his attention First he must be made to appreciate the fact that the condition will not become better but rather that it will progress As a result the pain will become worse and the patient will at the same time begin to experience systemic symptoms from absorption of toxic material It is also necessary to point out that his death will not occur quickly but that the process of becoming more and more of an invalid will be long drawn out During this period he will be a great financial burden to the members of his family as well as causing them marked mental anguish as they observe his suffering In almost all instances when the patient is faced with such a sequence of events he will reluctantly agree to the proper step

Aside from indicating the very unpleasant consequence associated with refusal to be operated upon it is also necessary to make all efforts to encourage the patient to take a realistic viewpoint regarding his problem and to permit the only therapeutic approach available under the circumstances It is well to point out that thousands of people who have also believed themselves incapacitated have resumed their daily occupations with the use of a prosthesis in a normal and efficient manner If it can be arranged it is worthwhile to have an amputee with a prosthesis discuss the matter of amputation with the patient at the same time demonstrating how capably he has made an adjustment to his difficulty Emphasis should be placed on the fact that amputation of one or even both lower limbs should not keep the patient from earning a living and enjoying many pleasures provided he has the will and determination to become rehabilitated

Factors Which Determine the Proper Time for Amputation

Ideally an extremity should be amputated when it is obvious that it can not be saved that there is no advantage to further delay and that the patient is in the best possible physical state However there are a number of factors which influence the decision either forcing premature amputation or delaying it beyond the propitious time

Presence of Uncontrolled Infection At one time the existence of a spreading superimposed infection that was resistant to available medical therapy necessitated immediate surgery as a life-saving procedure This was particularly true in the case of the diabetic individual with a nutritional disturbance who was prone to ascending lymphangitis systemic responses and acidosis Since the advent of effective antibacterial agents such a situation rarely arises Still when an uncontrolled secondary infection does exist there is no question that it should hasten the decision to amputate On the other hand the presence of a dermatitis or an associated ulcerated and infected area on the upper portion of the limb in the vicinity of the contemplated level of amputation may delay this step until the

cuts, so as to accelerate the process of healing and by so doing may actually cause progression of the nutritional disturbance For the same reason amputation of the limb may be performed before an entirely adequate trial of conservative therapy has been completed On the other hand one can not escape the fact that even with an ideal program, the result is not always satisfactory and the extremity may still have to be removed Or the gangrenous process may be halted but not in time to prevent the formation of a useless foot or leg because of destruction of important structures Under these circumstances the long period of disability and the financial cost may be wasted However, with increased experience in the proper choice of patients for conservative management, there should be fewer such failures

Major Amputation*

If despite intensive local and systemic therapy, the gangrenous lesion extends onto either the dorsal or ventral surface of the foot the likelihood of saving the extremity by continued conservative therapy is poor Such progression generally indicates that the thrombotic process is no longer limited to the digital arteries but has spread to the larger arcuate vessels of the foot As a consequence, adjoining toes can be expected to become gangrenous in a short while Under these circumstances further delay is not warranted not only because of the great expense but also because it will generally not alter the ultimate outcome Furthermore with involvement of larger quantities of tissue the patient may begin to show signs of absorption of toxic material from the affected site such as a rise in body temperature drowsiness and apathy Since it is not advisable to permit such a state to persist the patient should now be prepared mentally and physically for surgical amputation of the limb

Development of Proper Mental Attitude Toward Amputation

The *psychological preparation of the patient for the removal* of one or more of his limbs frequently is a difficult task This is especially so if the progression of the nutritional disturbance has been so rapid that there has not been sufficient time for him to become fully aware of the seriousness of his condition As a result when faced with a decision which if once consummated is irreversible frequently his first response is to say that he would rather die than permit the operation At that moment he is completely overcome by the seriousness of the problem confronting him It is for such a situation that the physician or surgeon needs all the tact patience and persuasiveness at his command If considerable pain is associated with the gangrene it may facilitate a more rapid acceptance of a realistic approach to the problem

For the patient who has been subjected to a period of conservative management only to learn that this has been unsuccessful and that amputation must now be carried out, the acceptance of such a decision is also very difficult By this

* Although this section is limited to the problems encountered in amputation of the lower extremities the discussion can also be applied to the relatively rare occasions in which removal of one or more fingers or even of a hand or forearm is necessary in the treatment of a peripheral vascular disorder

On this account as well as to control any local infection in the extremity the daily use of some broad spectrum antibiotic is indicated during the entire period of refrigeration and for a number of days postoperatively

Factors Involved in Determining Proper Level for Amputation

Through clinical trial several levels on the lower extremity have been found to be the best sites for amputation The first is at the base of individual toes as already discussed while the second is through the middle portion of the calf approximately 18 cm (7 inches) below the knee joint so as to leave 14 cm (5½ inches) of tibia The remaining two locations are on the thigh at the junction of its lower and middle third and through the supracondylar region Amputation through the foot is rarely attempted except for the transmetatarsal *operation* Removal of the leg and foot below the middle portion of the calf is of no advantage since a useful stump can not be expected Although the primary *aim in amputation* is the retention of the maximum amount of viable tissue still *in the* final decision regarding the site the above factors must also be taken into consideration Which of the commonly used measures should be performed on a specific individual can only be determined through a careful survey of all aspects of the problem as indicated below

Circulatory Tests There are several procedures for the determination of the state of the local circulation which are valuable in the elucidation of the proper level for amputation Among these is oscillometry which may give pertinent information regarding the location and degree *of block* in the arterial system If the readings obtained at the calf are only somewhat reduced (to approximately , units) the possibility of accomplishing a successful below the knee amputation is very good With such results *it can be assumed* that the occlusion is distal to the popliteal artery and that there is sufficient local circulation to permit healing of the stump Confirmatory evidence for such a view is the presence of palpable pulsations in the popliteal artery

Very low figures obtained at the calf although indicating that there is almost complete occlusion of the main arteries at this level do not necessarily rule out a below the knee amp*utation* inasmuch as the extent and efficiency *of the existing* collateral circulation can not be determined through the use *of oscillometry (p 45)* However if at the same *time* pulsations are absent in the femoral artery then this type of procedure is definitely contraindicated To obtain information regarding the state of the collateral vessels arteriography (Chap XXV) and the histamine *wheal test (Chap II)* are useful Even after evaluating the results of all *these* measures not infrequently it may still be difficult to deter*mine the proper* level for amputation and hence still other means must be utilized

Clinical Basis for *the Different Levels of Amputation* There is considerable controversy concerning the matter of amputating *below the knee In* arteriosclerosis obliterans it is the view of some workers[7] that since the underlying process is progressive a supracondylar *approach* is the logical choice Another argument in favor of such a decision is that *if a below* the knee amputation were performed and a good result did not occur *it would* mean that a second attempt at a higher level

lesion is controlled Otherwise the possibility of obtaining a successful stump is reduced

Pain At times excruciating pain as already mentioned will force amputation of an extremity before this is considered advisable on the basis of the severity of the nutritional disturbance alone It is assumed of course that all means to control the symptom have been found to be futile and there is no other alternative for preventing the rapid mental deterioration which would otherwise result Continued use of large quantities of narcotics merely accentuates the frequently existing addiction without materially controlling the pain Fortunately, such a set of circumstances does not occur often

Poor Physical State of Patient If the previous conservative management has been drawn out, the patient s physical state may have declined making him a poor candidate for surgery Frequently too the need for amputation occurs in elderly debilitated individuals who are suffering from anemia and inadequate diet Under these circumstances if at all possible it is advisable to delay the operation until the general physical condition of the patient is built up by means of blood transfusions intravenous fluids and adequate protein and vitamins in the diet

If removal of the gangrenous limb is imperative because absorption is producing systemic responses time can be gained for the institution of adequate preoperative treatment through the use of refrigeration This is carried out in the following manner

As soon as the site of amputation is determined the extremity is covered with finely cracked ice up to a level some distance below the selected location for local freezing may interfere with subsequent wound healing Whether or not a tourniquet is of value has not been settled If used it should be applied several inches below the upper level of application of ice and only after several hours of refrigeration so as to permit the development of adequate anesthesia To maintain the limb in constant contact with ice a bag of oiled silk or rubber sheet is so adjusted as to permit drainage of the melted portion through a tube inserted at the inferior angle of the container Elevation of the head of the bed facilitates this action Sand bags or pillows are placed along the sides for support and blankets are used to insulate the bag from the surrounding air

Electric refrigeration[17] obviates some of the difficulties associated with the use of cracked ice The apparatus is mounted within a portable soundproof cabinet and placed under the bed and from it an insulated tubing is led to a small freezing unit on the bed Before the limb is placed in the machine the portion which remains outside the unit is wrapped in a heavy felt pad An automatic relay device maintains a constant temperature of $-18°$ C ($0°$ F) for the first few hours until sensation is lost and then the level is raised to $-4°$ to $-1°$ C ($25°-30°$ F) for the more prolonged period of exposure

The therapeutic effects from refrigeration are almost immediate The measure causes disappearance of pain and such signs of toxicity as fever and a rise in pulse rate and respiration Although it is rarely necessary for longer than 48 hours no ill effects will result from a prolongation of the procedure for several more days The only objection is that while it is being carried out the patient must lie continuously on his back and thus becomes susceptible to a hypostatic pneumonia

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examination of the limb would lead one to believe Under such circumstances transmetatarsal amputation may be attempted provided the ulcer or gangrene has not extended for any distance onto the foot and the inflammatory process can be controlled by antibacterial therapy [14] However this procedure must be done with the thought in mind that a higher amputation may still have to be carried out Hence only the patient who is considered to be in such physical shape that he can undergo two operations if necessary should be subjected to transmetatarsal amputation

In summary the determination of the proper site of amputation should rest on the results with the various tests and the clinical judgment of the doctor If there is any question as to how the patient might respond systemically to surgery the procedure should be carried out above the knee Even when there is a possibility that the latter structure could be preserved the ultimate decision should be left in abeyance and the patient prepared for both types of operations A trans metatarsal amputation should be considered for a very limited number of patients

Complications of Amputations*

Nonhealing of Stump As in the case of the original lesion two factors may contribute to the lack of healing of the stump the existence of infection and the presence of an inadequate local circulation Although with our present refinements in technic and asepsis and the prophylactic use of antibacterial agents the inci dence of wound infection has been markedly reduced at times it is still necessary to cope with such a situation This is particularly true if the ulceration or gangrene of the foot was originally associated with a severe infection leading to lymphangitis and regional lymphadenitis On occasion even gas gangrene may develop

In the treatment of infection of the stump the first step is prophylaxis This in volves the use of penicillin or other antibiotics for at least one week before opera tion in order to help destroy any bacteria which have penetrated the tissues some distance proximal to the gangrenous material The medication should then be continued for 10–14 days after surgery to prevent infection of the stump from the dressings At the time of operation care in tying off all bleeding points and in reducing oozing and accumulation of serum in the wound will also help protect the tissues from infection Attempts to reduce the amount of tissue subjected to trauma or crushing or made ischemic by ligatures will likewise decrease the inci dence of infection

In the active treatment of the condition the measures used will depend upon the degree of involvement If the infection is limited to the edges of the wound local application of antibacterial agents and cleansing solutions together with parenteral use of antibiotics is generally adequate to control the situation How ever if signs of inflammation are noted over a considerable portion of the stump and if marked swelling and pain are present it can be assumed that the infection is deep and extensive Under such circumstances it is necessary to open the entire length of the incision and evacuate the pus and other products resulting from liquefaction of involved tissues The removal of the necrotic material may then be

* For a discussion of phantom limb see C usalgic States Chap XVIII

would then have to be done Patients with arteriosclerosis obliterans as a group are poor surgical risks in any case and subjecting them to two operations markedly increases the hazard Furthermore, the aim of making the patient self sufficient and a wage earner is not as important a consideration in these individuals as in the case of younger patients Besides, a prosthesis applied to a supracondylar or midthigh stump is generally adequate for the performance of the limited physical activity normally required in this age group

On the other hand in the young individual with thromboangiitis obliterans the importance of saving the knee joint is obvious, and hence the possibility of removing the limb without sacrificing this structure should not be dismissed unless the physical findings indicate little chance for a successful outcome In this regard it is well to remember, too, that a below the knee amputation is attended with a relatively lower mortality than are those performed at the midthigh or supracondylar levels [20]

It has been suggested that a preliminary sympathectomy will help in the healing of the stump when a below the knee amputation is contemplated However, as already mentioned subjecting an individual who is in poor physical shape to two or even possibly three operations instead of one increases the risk considerably Moreover in the case of the patient with arteriosclerosis obliterans who frequently demonstrates advanced organic degeneration loss of elasticity of collateral vessels and only slight vasospasm, it is very doubtful as to whether sympathectomy will extend the level of safe amputation any more effectively than general supportive measures [1] Of course in the young individual with thromboangiitis obliterans such a procedure has more in its favor since this type of patient is generally in better physical state to withstand two operations

State of Tissues Surgically Exposed If despite the use of the above criteria, there is still some question as to the proper site of amputation it is advisable to attempt the procedure below the knee first at the same time preparing the patient surgically for a higher amputation if this becomes necessary As the operation proceeds if free bleeding and oozing from small vessels in the skin and muscle is only minimal if the main arteries are completely obliterated and of greatest importance if the muscles appear friable and brown in color then it will probably be expedient to change the operative site to above the knee and perform a supracondylar or midthigh amputation On the other hand the presence of brisk bleeding partially patent large arteries through which blood is flowing and a red healthy appearance to the muscle structures should all support the belief that the proper site had been selected for amputation (For actual technic involved in the different procedures the reader is referred to a book on surgical vascular procedures)[1]

Role of Infection If infection plays an important role in the progression of the nutritional disturbance as in the presence of diabetes the decision with regard to level of amputation rests on several other factors besides the ones already enumerated In many such instances the appearance of the foot is misleading since some of the changes are still reversible if the secondary infection can be halted in time In other words part of the destruction of tissue is due to the latter factor while the impairment in local circulation is actually not as marked as a superficial

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facilitated by continuous or intermittent irrigation with Dakin's solution, or the application of *Azochloramid in oil, Tryptar* or *Varidase* Only when granulating tissues begin to cover the exposed surfaces of the wound should secondary closure be considered Until then it is best to keep the lesion open to prevent the formation of pockets of pus In order to remove irritating secretions and necrotic material, the daily use of whirlpool baths with tincture of green soap is worthwhile At all times care should be taken to prevent recontamination of the wound or the introduction of new secondary invaders

The rare case of gas gangrene requires immediate intensive therapy This involves opening the wound wide, giving large doses of gas gangrene antitoxin and penicillin or other antibiotics At the same time the patient should receive supportive treatment including the inhalation of oxygen When the infection appears *controlled reamputation should be done In most instances the prognosis is very* grave since the patient is generally old and his resistance to a virulent infection is low

Inadequate local circulation is much more frequently responsible for nonhealing of the stump than is infection Its presence indicates either that the site for operation had been poorly selected or that the surgical procedure had been unnecessarily traumatizing resulting in an exaggeration of already existing tissue anoxia Of course in certain circumstances there may be no alternative but to attempt an incision through structures which are obviously in a precarious state of nutrition

The treatment of a stump which has failed to heal because of lack of local blood flow will depend upon the degree of destruction of tissue In the presence of extensive gangrene, *the best approach is to reamputate* as soon as the physical state of the patient will permit this Otherwise there may be absorption of toxic materials from the site as well as spread of the thrombotic process into the vessels of adjoining normal structures thus reducing the chances of a subsequent successful result *However if the necrosis is limited to the skin edges or even to part of one* of the flaps without any apparent involvement of deeper tissues it is best to wait in order to determine whether or not the process will become stationary If this occurs the gangrenous material can be removed later and perhaps skin grafting performed to facilitate healing or epithelialization may take place spontaneously All during the prolonged period of treatment the wound should be cared for aseptically and the patient should be receiving parenteral antibacterial therapy

After an adequate period of intensive conservative treatment if the stump does not heal or there is involvement of adjoining normal tissue reamputation will have to be performed Where the original site was below the knee such a procedure does not pose any particular problem However when a supracondylar or midthigh amputation is unsuccessful difficulty is usually encountered in obtaining a suitable site for reamputation Certainly under these circumstances the possibility of being able to use a prosthesis on the resulting stump is slight In some instances it may even be necessary to disarticulate the entire lower extremity in order to obtain *healing*

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blood in the abdomen must be supported by the valves in the external iliac and femoral veins. In individuals in whom valves are also absent in these two vessels, an even greater burden of support is placed on the valve at the saphenofemoral junction. It is for this reason that varicosities in the lower extremity are usually due to incompetency of the valve at this junction.

Other Conditions Interfering with Venous Return. Aside from prolonged standing there are several other factors which reduce venous return from the lower extremities and hence predispose to varicosities. These include heavy muscular work with straining at lifting, repeated straining at stool, pregnancy, and pelvic tumors, all of which increase intra-abdominal tension. Constriction of the limb by elastic supports, girdles, garters, and tight bandages has a similar effect. Obesity may also contribute to venous stasis since subcutaneous fat supplies little effective support to the superficial veins.

Age. Actual varices rarely appear before adolescence for several reasons. First, the hydrostatic pressure reaches its maximum only when full height has been attained.[16] Second, in early youth the elasticity of the skin over the veins is greater than in later life and the diameter of these vessels is relatively smaller, all of which tend to prevent venous distension. Finally, muscular movements are more active and constant in early youth, thus reducing venous stasis. At the same time occupations involving protracted periods of standing are rare in this age group.

Although in most instances severe varices have their inception after adolescence and before the age of 30 years, rarely do the majority of patients present themselves for treatment until they have reached the fifth or sixth decades of life.[7] This is probably due to the fact that with age the venous walls and valves lose their tone and begin to fail. The resulting increase in symptoms compels the individual, who had previously neglected his condition, to seek medical advice.

Sex. Varicosities are predominantly present in females, perhaps because pregnancy is a potent agent in initiating and aggravating them. However, a 2 : 1 ratio has also been reported in series in which pregnancy did not play an important role. It is possible that anatomic factors, such as the broader pelvis in the female with more angulation of the vascular structures, and the increased engorgement of the pelvic veins during puberty, menopause, menstruation, and pregnancy hasten the development of varicosities.

PATHOGENESIS

When the valves* in the veins of the lower extremities become incompetent, regurgitation of blood will occur into the superficial venous system, producing varicosities. Depending upon the site of involvement, this reflux will take place either through the saphenofemoral junction or through communicating or perforator vessels which join the two systems at various levels in the thigh and leg. As a result of the marked distension of the superficial veins and the poor support they possess, these vessels enlarge and become tortuous, in the process of which the valves locally also become incompetent. It should be emphasized that only the veins lying in the superficial fascia and surrounded by fat are prone to this type of

* For discussion of these structures, see Venous Valves, Chap. XXVI.

CHAPTER

XIII VASCULAR DISORDERS AFFECTING THE VENOUS SYSTEM

I DISEASES OF THE SUPERFICIAL VEINS

PRIMARY VARICOSITIES

Varicosities are one of the most important afflictions of the venous system, as well as one of the most common of the peripheral vascular disorders In fact the *majority of the patients ordinarily seen in a peripheral circulatory clinic are either* suffering from this condition or from its complications particularly ulceration It has been estimated that 60 per cent of patients of the age of 40 and above who are active on their feet will have some pathology of the venous system [1] Furthermore 80 per cent of women after their third pregnancy manifest such changes

Varicosities can be divided into the primary or idiopathic type and those which are secondary or compensatory to such diseases as deep thrombophlebitis and acquired or congenital arteriovenous fistula The following section deals with primary varicosities, while the other category is discussed elsewhere (See *Dilated and Varicose Veins* Chap XVI and *Clinical Characteristics* of acquired arterio *venous fistula* Chap XVII)

Etiology

Congenital Weakness One popular explanation for the production of incom petency of the venous valves is an inherent structural weakness of the veins them selves *a type of constitutional defect In support of such a belief* is the recent anatomic finding that in some patients smooth muscle and internal elastic mem brane may be absent in the valve area of the great saphenous vein at the sapheno femoral junction [16] Furthermore a familial history of varicosities is frequently ob tained However it must be noted that strong evidence for the existence of a hereditary basis has not been forthcoming

Erect Position There is little quesion that mechanical or hemodynamic factors play an important role in the production of primary varicosities The most impor tant of these is the high hydrostatic pressure to which the veins of the lower ex tremities are subjected as a result of the assumption of the erect position Since there are no valves in the inferior vena cava and common iliac veins the column of

one must consider the possibility of incompetency of the tributaries of the great saphenous vein (Fig 28B) In this regard involvement of the lateral superficial femoral vein manifests itself as varicosities situated on the anterolateral aspect of the thigh while incompetency of the medial superficial femoral vein produces a similar type of change on the medial and posterior surfaces

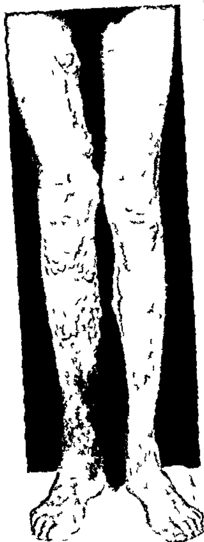


FIG 8 (*Continued*) C Marked varicosities of entire length of great saphenous vein Pigmentation (sign of venous stasis) also noted

In the case of the small saphenous vein the location of the varicosities will depend upon the level at which the vessel penetrates the calf to join the popliteal vein This may take place at any point between one third and two thirds of the distance from the popliteal crease to the ankle joint Generally the distended vessels are located on the posterior surface of the lower portion of the calf extending toward the heel and around to the lateral aspect of the ankle and dorsum of the foot The upper part of the calf may be free of varicosities

CLINICAL CHARACTERISTICS

Local Signs and Symptoms The patient suffering from primary varicosities may have no symptoms at all or he may complain of a sense of heaviness fullness and easy fatigue in the involved leg particularly when he is standing in one position for any period of time Although the pain may be dull at first, it may become acutely sharp and stabbing finally forcing the patient to lie down and elevate his extremities Walking may also reduce the complaints but not to the same degree Night cramps are fairly common and appear to some extent to be related to the amount of physical exertion indulged in during the day Another finding is swelling of the ankles which forms with activity and disappears after a night s rest Generally there is no correlation between the severity of the symptoms and the size and extent of the varicosities

Systemic Responses In some elderly patients a moderate degree of varicosities persisting over a period of years may cause cardiovascular symptoms particularly if there is an underlying reduction in cardiac reserve The explanation is that such individuals are unable to cope effectively with the increase in venous return and rise in central venous pressure which occur each time the recumbent position is

change In contrast, the deep vessels are located in an osteofibrous compartment receiving additional support from the connective tissue sheath that closely surrounds both vein and artery



FIG 28 Primary varicosities in different sites A Involvement of great saphenous vein B Varicosities of tributaries of great saphenous vein

LOCATION OF VARICOSITIES

Either the great saphenous or the small saphenous venous system or both may be affected In the case of the great saphenous vein the varicosities are generally located on the medial side of the thigh and leg *extending both anteriorly and posteriorly* (Fig 28A and C) If varices are present on other portions of the thigh

nous blood contains greater than normal amounts of oxyhemoglobin and there is an increased cutaneous temperature proximally Furthermore in the course of making a *venous pressure reading* pulsations may be noted in the glass tube which are synchronous with the heart beat However a bruit and thrill are generally absent An important *differential point* is the great incidence of recurrence when the lesion is misdiagnosed and treated surgically as an uncomplicated case of primary varicosities (For further discussion on this subject see *Congenital Arteriovenous Fistula* Chap XXIII)

TREATMENT OF PRIMARY VARICOSITIES

MEDICAL THERAPY

General Considerations

Medical management of primary varicosities generally has limited value, since the procedures at best alleviate rather than cure the disorder Under certain conditions however such an approach is necessary either as a temporary measure or permanently if there are definite contraindications to surgery

Among the conditions in which medical means are advisable is pregnancy Usually varicosities will appear during this state or if already present will become more marked Since they frequently tend to regress or even disappear after delivery it is best to delay surgery until the element of venous obstruction contributed to by the pressure of the uterus on the pelvis and by the increased vascularity of the pelvic veins is eliminated In the meanwhile it is necessary to control the progressing distension of the superficial veins by some type of compression bandage However it must be pointed out that pregnancy does not contraindicate surgery if the severity of the varicosities warrants it and if medical measures can not adequately control the condition

The temporary use of medical therapy should also be considered in a number of other situations In the case of nonsymptomatic minor varicosities it is probably advisable to delay surgery and thus determine whether or not the condition is progressive Varicosities in the presence of marked obesity should likewise be treated conservatively until the patient has responded to a low calorie diet The weight should be reduced to at least 200 pounds before operation is attempted

Certain types of individuals should continue to use medical methods permanently to control their varicosities The patient in whom recurrences have taken place after several corrective operations falls into this category This is particularly so if he is very hesitant to subject himself to another operative procedure which again may not be successful The same approach is also indicated in some psychoneurotic individuals

There is some question regarding the advisability of operative intervention for varicosities in the case of the elderly patient Certainly the one who has an associated occlusive arterial vascular disorder or a severe vasospastic state affecting the lower extremities should be treated conservatively It is clear for example that a procedure involving multiple incisions on a leg with an impaired arterial circulation might lead to the formation of ulcerations which in all probability would not heal Still it is essential to control the venous stasis in such a limb since this state tends

assumed[10] Such changes are the result of an increase in circulating blood volume which exists in the long standing case of varicosities (p 407) On the other hand if this compensatory change in circulating blood volume is not adequate, then cardiac symptoms may be experienced when the patient stands for any period of time[3] These consist of shortness of breath, now relieved in the recumbent position, mild precordial pain, and dizziness Removal of the peripheral blood reservoir by surgical means restores the hemodynamics of the patient toward normal and reduces his complaints[3]

Differential Diagnosis

Distinguishing Points Little difficulty should be encountered in making the diagnosis of primary varicosities Of importance are (1) the appearance of prominent tortuous superficial veins on the assumption of the upright position and at times even in the horizontal position (Fig 28) (2) the presence of a regurgitant flow in these vessels as determined by the various tests devised for this purpose (Chap V) and (3) the history of the initiation of symptoms with prolonged standing However, attention must be called to the fact that varicose veins are not always apparent particularly if there is a considerable deposition of subcutaneous fat or if there are changes in the consistency of the skin Signs of venous stasis may be present but these are not pathognomonic, since they may be associated with other entities

Secondary Varicosities Primary varicosities must be differentiated from those that follow an attack of deep thrombophlebitis or from those due to an arterio venous aneurysm In the case of thrombosis of a main deep venous channel generally a history reveals the acute episode followed by the appearance of the varicose veins At times it may be necessary to resort to venography to demonstrate the presence of a block in the involved vessel and the existence of bridging collaterals Such findings are never noted in the case of primary varicosities The various tests for competency and patency of the deep venous system (Chap V) may also be of value in the differential diagnosis between primary and secondary varicosities Although determination of venous pressure in the lower extremity following exercise is useful such a procedure is rarely performed in the office or at home (For the differences in venous pressure observed in the two conditions, see *Venous Pressure Measurements in the Lower Extremities* Chap XXV)

Secondary varicosities associated with a traumatic arteriovenous fistula are no real problem in differential diagnosis The history of trauma to the limb followed by the appearance of the varicosities and the presence of the characteristic signs of this lesion—the existence of a pulsating mass in the vicinity of the injury the continuous bruit the thrill and the changes in skin temperature proximal and distal to the lesion—should all help (For further discussion see Chap XVII)

Varicosities due to arterial varices offer much more difficulty in their differentiation from primary varicosities In this condition the dilated vessels appear rather suddenly[11] Their location is on the lateral or less often posterior aspect of the leg rather than at the classical site on the medial aspect When the limb is elevated the veins empty incompletely and never as rapidly as do primary varicosities As with traumatic arteriovenous communications venous pressure is high ve

used Ace bandage either 7 5 or 10 cm (3 or 4 inches) wide It is applied over the entire foot except for the toes and wound spirally around the ankle and leg up to the knee Attempts to continue the application around the knee and up onto the thigh are not satisfactory since generally the bandage loosens even with a little activity The use of two separate bandages one on the leg and the other on the thigh with the knee free is somewhat better although the upper one soon becomes ineffective in controlling venous stasis Another disadvantage to an Ace bandage is that it rapidly loses its elasticity thus necessitating frequent substitutions It has one advantage over an elastic stocking in that the amount of compression of the leg and foot can be altered to suit the requirements On the other hand it is more unsightly

Another type of compression bandage has recently been described consisting of two layers the first a Webril cotton roll and the second a 10-cm (4 inch) wide elastic bandage made of densely woven lastex (see Appendix)[8] The foot of the patient is held by an assistant at a 90 degree angle to the leg and the knee is flexed at a 15 degree angle The cotton bandage is started at the level of the head of the first metatarsal bone and is applied about the long axis of the foot and leg to a level just above the tibial tubercle Additional padding is placed over the malleoli Achilles tendon and anterior aspect of the tibia and the second layer is applied in a similar manner Then the patient is instructed to walk several blocks If pain is present the elastic bandage is readjusted for otherwise painful pressure may occur over the bony prominences

The one drawback to all elastic supports is that where bony and tendinous elevations are located in the leg and around the ankle effective uniform pressure can not be obtained in the depressions between them[23] Since these sites are situated in the distal portion of the extremity where venous stasis would ordinarily be most marked such a defect may defeat to some extent the purpose of the supports

Injection Technic

Another medical measure which is used in the control of varicosities is the injection of sclerosing solutions into the affected veins only cases showing minor involvement are satisfactorily treated by such means The procedure does not alter the reflux of blood and hence as one set of vessels is obliterated another becomes more prominent as a result of blood being shunted into it Furthermore recanalization of the thrombosed veins themselves will eventually occur due to the constant back pressure However the method does have a definite place as a supplement to surgical therapy for it can be subsequently used to occlude those channels which are still prominent after operation In some instances it is also utilized at the time of vein ligation to produce an intimal irritation which then causes clotting intimal adherence and finally fibrosis

Untoward Responses Although it is true that the injection method permits the patient to be ambulant the procedure is not without danger First there may be various types of allergic reactions to the sclerosing agent varying from minor urticaria to angioneurotic edema asthmatic dyspnea and even severe anaphylactic

to counteract the movement of blood from arterioles into capillary beds, thus exaggerating the existing chronic anoxia In most instances the removal of stagnant pools can be accomplished by the use of a compression bandage However, in some cases such a procedure may aggravate the arterial insufficiency by causing enough pressure on the small vessels to decrease the quantity of blood reaching the tissues thus producing pain This is a warning to discard the compression bandage If control of venous stasis is still deemed necessary some type of simple surgical procedure should be performed, in which skin incisions are limited to the thigh and no sclerosing solutions are used

Elastic Compression

Compression of the superficial veins can be accomplished by the use of elastic stockings and bandages made of cotton and reinforced with elastic strands Elastic stockings are the most widely used of this group

Elastic Stockings The type which has a heel and covers a good portion of the dorsum of the foot up to the base of the toes is much more comfortable to the patient than one which has only a strap like arrangement Careful fitting of the stocking is essential To do this the extremity should be measured at various levels and the appropriate size obtained from stock If the limb is unusually shaped it is advisable to make the stocking to order for one which is too tight or too loose will be of little value and may be harmful

The length of the stocking will depend upon the extent of the varicosities If the involvement appears to be limited to the leg a stocking which ends below the knee is adequate However, if there are obvious dilated channels on the thigh then one which also encompasses this portion of the limb is preferable In the past it was generally necessary to make such a stocking to order since the ones obtained in stock tended to slide down and wrinkle up at the knee, thus defeating the purpose for which they were being used At present however a satisfactory full length stocking is available commercially this can be pulled over the thigh and kept in place with a garter belt The models are made to stretch either in one or two directions and are composed of either heavy or light weight material In the presence of associated edema of any marked degree the former should be used There are also nylon elastic stockings but these are not as practicable as the others Ordinarily with the usual precautions the heavy weight stocking can be expected to be effective for about 6–7 months while for the light weight type the period is about 3–5 months Care in washing the stockings so as not to injure the elastic fabric will prolong their usefulness Purchasing a pair for each extremity is also of value in this regard

In slipping the stocking on the patient should be instructed to turn it inside out down to its foot Then he places his foot in the stocking foot with his heel resting in the stocking heel The stocking leg is carefully worked over the patient s heel and up on his leg Each section should be in place before the remainder of the stocking is pulled up further Carefully drying the foot and leg and then applying talcum powder to the skin may help facilitate this

Elastic Bandage The simplest type of compression bandage is the commonly

used Ace bandage either 7.5 or 10 cm (3 or 4 inches) wide It is applied over the entire foot except for the toes and wound spirally around the ankle and leg up to the knee Attempts to continue the application around the knee and up onto the thigh are not satisfactory since generally the bandage loosens even with a little activity The use of two separate bandages one on the leg and the other on the thigh with the knee free is somewhat better although the upper one soon becomes ineffective in controlling venous stasis Another disadvantage to an Ace bandage is that it rapidly loses its elasticity thus necessitating frequent substitutions It has one advantage over an elastic stocking in that the amount of compression of the leg and foot can be altered to suit the requirements On the other hand it is more unsightly

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Untoward Responses Although it is true that the injection method permits the patient to be ambulant the procedure is not without danger First there may be various types of allergic reactions to the sclerosing agent varying from minor urticaria to angioneurotic edema asthmatic dyspnea and even severe anaphylactic

shock Second, the possibility of a marked degree of local chemical thrombophlebitis must always be considered, at times this may progress to involve the deep as well as the superficial veins On occasion such an extension may lead to pulmonary embolism 6–10 days after the use of a sclerosing solution [4] Very rarely the complication may be noted within a few minutes after the injection [7] Another untoward effect may result from a leak of the material out of the vein into the surrounding tissues to cause aseptic necrosis and slough A similar change may follow *erosion of the vessel wall due to the administration of* excessive amounts of the solution The chemical thrombophlebitis may also act as an irritable focus to initiate arterial spasm and thus reduce the caliber of the arterial tree or its collateral bed to a critical degree

Since some of the above responses might have very serious consequences in the presence of arterial insufficiency, it is clear why a knowledge of the state of the local circulation is essential before attempting any injection procedures

Types of Sclerosing Solutions An ideal sclerosing agent has not as yet been developed although a number of substances have had extensive clinical trials They can be divided into three groups hypertonic solutions soaps and cytoplasmic poisons [17] The hypertonic solutions which act both by causing dehydration *through osmosis and by producing irritation of the intima of the vein consist* of such substances as 50% glucose 20–30% sodium chloride and 20% sodium salicylate Of the soaps there are 5% sodium morrhuate 5% sodium ricinoleate and 5% sodium ricinoleate Examples of cytoplasmic poisons are 5% quinine hydrochloride with and without urethane quinine urea *hydrochloride* and bichloride of mercury 1 2000 Of all the above agents sodium morrhuate is probably employed most often

Preliminary Steps Before the injection is carried out it is necessary to determine whether or not sensitivity to the sclerosing solution exists This is accomplished by injecting 0 25 cc of the material into a small vein preferable twenty four hours prior to the procedure If a reaction occurs another solution should be substituted Even greater precautions should be taken with patients who have had injection therapy some time in the past In fact it is advisable to begin testing with a solution not previously used since such individuals appear to acquire sensitivity to the original agent if a long period is allowed to elapse between treatments

Technic Either empty or full vein technic may be used The former consists of having the patient lie down with the leg in dependency so as to distend the vessels Then the needle is inserted into the vein and the limb is elevated to drain the blood out At this point the sclerosing solution is injected If a maximum effect is desired, tourniquets should be placed above and below the segment to be treated just before the material is injected into the collapsed vein Such a step is desirable when dealing with distended vessels

In the full vein technic the patient either stands on a stool with the operator sitting in front of him on another stool or he may sit on a table with the leg in dependency The latter has some advantage since the subject who is standing may become faint when the sclerosing solution is injected With both of these positions the varicosities are brought into prominence facilitating insertion of the needle

At the same time however the resulting large quantity of blood in the distended veins causes dilution of the sclerosing solution which counteracts to some degree the desired effect particularly if large varicosities are being treated

The area is cleansed with an antiseptic and the injection made through healthy
A 5 cc syringe is used with a sharp
-1 inch) in length After the needle
to make certain that the lumen has

been entered and then the material is injected rapidly No more than 3 small veins or 1 large vein should be treated at one time and the total quantity of agent used should not exceed 4 cc In each instance as the needle is withdrawn a sterile gauze pad previously prepared is placed over the site of injection and held firmly in place by adhesive strips An elastic bandage is applied over the entire leg and the patient is instructed to walk at once The support holds the large varices collapsed so as to facilitate thrombosis which occurs during the 24 hours after injection If the reaction is severe the bandage should be left on for several days The gauze pad may be removed after 12 hours

SURGICAL THERAPY

In most instances of symptomatic varicosities of moderate or marked degree a surgical approach is indicated This is particularly true if any of the signs of venous stasis are present However as pointed out elsewhere (p 285) in the presence of ulceration it may be necessary to delay the operation until infection has been controlled The main purpose of surgical therapy is to produce complete obliteration of the principal components of the involved saphenous systems That this aim is not always accomplished is supported by the relatively high percentage of recurrences of varicosities following operation

Despite the frequent indication for surgical treatment considerable difference of opinion still exists as to which procedure is most efficacious Even in large vascular clinics there is no general agreement on this point In fact frequently the various services in the same hospital will simultaneously be using several different operative measures The methods most frequently attempted are (1) high ligation of the great saphenous vein at its junction with the femoral vein (2) high ligation of the great saphenous vein follo
agent into the distal portion of
vein at its junction with the fe
ligation and division of the vessel along its course and (4) high ligation of the great saphenous vein and extirpation of a part or all of this vessel using a stripper Percutaneous methods of applying ligatures have also been used for the purpose of producing multiple ligations on the lower portion of the thigh and on the leg[8 17]

Preliminary Steps to Surgical Procedures

Before a surgical procedure is contemplated for the treatment of varicosities several steps must be carried out First it is necessary to demonstrate that the deep venous system is patent (Chap V) although there is some question as to how pertinent such information is to the problem Second the site or sites of

incompetency must be ascertained This involves determining the function of the valve at the saphenofemoral junction and of similar structures in the small saphenous system and in the communicating veins (Chap V) The exact location of incompetency and the course of the main superficial venous channels are marked out on the skin with a dye or indelible pencil so as to assist in the ligation of the involved vessels Finally, the state of the local arterial circulation should be studied (Chaps II and III) On the basis of the results obtained with the various tests, the proper course of treatment is then decided upon

Surgical Procedures

High Ligation of Great Saphenous Vein Alone Some workers are of the opinion that if the saphenofemoral valve is incompetent while the deep venous system is patent and the valves in the communicating veins are competent, high ligation of the *great saphenous vein is sufficient to control the varicosities At the* same time it is essential to isolate, ligate and divide several well defined venous trunks entering the bulb (p 426) and to remove 4-6 cm of the main vessel, for *otherwise there will be subsequent recanalization Another precaution is to* ligate the great saphenous vein as high as possible, to prevent formation of a varix in the proximal stump

Unfortunately the above procedure is followed by a relatively high percentage of unsatisfactory results even in cases in which there is no clinically demonstrable incompetence of communicating veins It is possible either that the tests are not always effective in detecting existing weaknesses or that the perforating branches may become incompetent after operation [9]

High Ligation of Great Saphenous Vein with Retrograde Injection This measure will generally give good results and in most instances there are fewer prominent veins requiring injection postoperatively than with some of the other methods *Still it is necessary to point out that the use of sclerosing solutions in conjunction with high venous ligation is associated with certain dangers and dis* advantages Aside from those already enumerated (p 227) such a procedure may cause *enough of a chemical phlebitis to compel the patient to remain in* bed thus defeating the ambulatory nature of the operation As a result of the various objections to sclerosing solutions there has been a definite tendency to abandon their retrograde injection in some of the large teaching hospitals [9]

Great Saphenous Vein Ligation and Multiple Ligation at Lower Levels The results with this method are generally good as far as the ultimate clinical picture is concerned However there may be a higher incidence of wound infections and poor wound healing since more skin incisions are performed and a larger area of lower extremity is necessarily exposed at operation

If the small saphenous vein is also found incompetent it should be ligated at the same time In fact it is the opinion of some workers that even when there is no clinically apparent involvement of this vessel (Chap V) the procedure should still be carried out Evidently the increased load placed upon it after ligation of the great saphenous vein is in some instances sufficient to cause it to become *incompetent* subsequently

Vein Stripping Extirpation of the great saphenous and small saphenous veins with a stripper should give good results in most instances although it must be pointed out that this is the most formidable of all the surgical procedures The fact that frequently the operation is associated with a considerable amount of discomfort makes it necessary to use a general anesthetic or a spinal or caudal block instead of local infiltration with procaine Postoperative pain and tenderness will also delay the period of early ambulation and the return to work

Summary It is necessary to emphasize the fact that in the surgical approach to varicosities the use of a stereotyped operation should be avoided Instead the procedure should be aimed at blocking all important existing venous incompetencies as determined by the available tests One measure that is consistently performed is high ligation at the fossa ovalis and segmental excision of the great saphenous vein and all its tributaries at this level Additional ligations and excisions lower down on the thigh or leg should be done if incompetent veins are present at these levels Stripping may be substituted since it gives a better cosmetic result which obviously is important Furthermore it is followed by more extensive thrombosis of the numerous perforating branches since these are all torn by the stripper Multiple ligation does not accomplish this but on the other hand the postoperative pain and disability are much less than with stripping Retrograde injection of sclerosing solutions at the time of surgery is not recommended However there is no objection to the use of such agents several weeks after operation to obliterate the remaining incompetent vessels

Causes for Failure Following Surgery

A number of reasons have been suggested for the large percentage of recurrences of varicosities following the various types of operative procedures The main failing is neglecting to dissect out and ligate separately all the tributaries entering the great saphenous vein at the fossa ovalis The fact that at times these vessels have anomalous locations contributes to this situation If some of the veins are left intact there will be a shunting of blood through them into the distal segment of the great saphenous vein and as a consequence this vessel will become recanalized Recurrences may also follow division and ligation of the great saphenous vein at too low a level with persistence of an incompetent lateral superficial femoral vein This results in rapid canalization of the great saphenous system and the reappearance of varicosities A similar response will be noted after ligation of the great saphenous vein without removal of a segment of vessel due to the re-establishment of a channel directly through the ligated portion of vein Another cause for recurrences is failure at the time of operation to eradicate all the incompetent com [illegible]

[illegible] point which may be neglected is an examination of the small saphenous system Obviously if this is incompetent ligation of the great saphenous vein at the fossa ovalis and elsewhere will be of no benefit Another possibility is the presence of a pelvic tumor or some other mechanical obstruction of the main venous channels which raises the venous pressure in the vessels of the lower ex

tremity Under these circumstances vein ligation will not control the varicosities unless at the same time the underlying cause is removed Finally, as already mentioned (p 224), recurrences in a small percentage of cases may result from the failure to differentiate varicose veins due to arteriovenous connections of a congenital nature (*arterial varices*) from primary varicosities

Even after all diagnostic information is available and appropriate surgical procedures have been carried out recurrences may still take place These are seen most often with ligation of the great saphenous vein alone less often when this procedure is combined with multiple ligation of perforators and least often following vein stripping However, even with the latter procedure there is always the possibility that new channels will form which will bridge the gap between the proximal stump and lower segments of the venous system

It must be realized that no surgical procedure for the correction of varicosities actually produces a cure At best it merely improves the state of the venous circulation At the same time a greater than normal load is placed on the remaining congenitally weak veins which previously had demonstrated no signs of impairment In the true sense the formation of varicosities in such vessels can not be considered a recurrence of the condition but rather an extension into and involvement of, other veins

Complications and Sequelae

Thrombophlebitis A relatively frequent complication of varicosities is thrombosis of involved veins associated with phlebitis Because of the vulnerability of the distended vein to trauma such a vessel should never be used for intravenous medication In fact in a limb demonstrating any varices not even a normal appearing vein should be subjected to this procedure (For treatment of thrombophlebitis of varicose veins see p 236)

Hemorrhage Another complication of varicosities is gross hemorrhage from large thin walled superficial veins (Fig 29) This may follow slight trauma or even occur spontaneously Although most patients with varicosities are often fearful of such a possibility actually bleeding is a relatively rare occurrence The reason may be that by the time the skin has thinned out and the vein gives the appearance of being just beneath the surface thickening and strengthening of the vessel will have already resulted due to a local periphlebitis The varicose vein which is liable to hemorrhage generally has not been the site of any infection and it can be seen through the thin skin like a small blue marble [14] Loss of blood from a ruptured varix may be considerable and therefore attempts should be made to deal with it at once Elevation of the leg high on pillows and the application of a smooth snug bandage from the toes to a point above the site of the lesion should control the bleeding Rarely are there any complications like secondary infection or ulcer formation Prophylactic measures in the form of protective coverings over vulnerable sites should be employed to prevent further episodes of hemorrhage

Changes Associated with Venous Stasis The most serious complications of varicosities are those due to long standing venous stasis Among the more important of these are ulceration stasis dermatitis pigmentation and chronic indurated

cellulitis A full discussion of these abnormalities and photographs of typical lesions can be found in Chapter XVI

Subcutaneous Calcinosis A relatively infrequent complication of long standing varicosities is the deposition of calcium in and outside the involved veins Such a change is generally found in female patients who are past 60 years of age and who have had repeated attacks of acute thrombophlebitis in the varicose veins Roentgenograms of the lower extremities using exposures in two planes are of value in revealing the presence of the condition Not infrequently the calcium deposits can be palpated through the skin and on occasion they may even penetrate the cutis, thus tending to initiate a stasis ulcer



FIG 9 Complication of varicosities Erosion of varicose vein on right leg with hemorrhage

PROGNOSIS

The prognosis of the patient with varicosities depends in great part upon whether or not the complications associated with venous stasis can be prevented from occurring or if present whether or not they can be controlled and eliminated Although they may be temporarily disabling they are never associated with any immediate danger to life However in some instances they may result in a partial state of chronic invalidism

THROMBOSIS OF SUPERFICIAL VEINS

Thrombosis of the superficial veins in the limbs is a relatively frequent occurrence In the lower extremities the branches of either the great or small saphenous system may be affected while in the upper, the process may be found in the cephalic or basilic veins or in their tributaries

Clinically two different types of superficial thrombophlebitis exist The more common entity is superficial benign thrombophlebitis *in which a superficial vein* alone or in conjunction with some of its tributaries is the site of a thrombotic process The other, thrombophlebitis migrans is a relatively rare condition characterized by occlusion of small segments of superficial veins in one or more extremities It resembles the changes in the veins observed in the early stage of thromboangiitis obliterans

In general thrombosis of superficial veins does not produce any significant systemic reaction even when the involvement is extensive Edema of the affected extremity is likewise absent since there is no obstruction in the main venous channels and hence no significant impairment in venous return However on occasion thrombophlebitis *migrans is associated with deep venous thrombosis* and under such circumstances swelling is present as well as mild fever and malaise

SUPERFICIAL BENIGN THROMBOPHLEBITIS

Introduction

Etiology Superficial benign thrombophlebitis may be caused by a number of different agents Among these are injury to the vessel wall following trauma to the limb the intravenous injection of hypertonic or sclerosing solutions venous stasis due to varicosities and local inflammatory processes in the vein wall At times no apparent factor can be elicited for the initiation of the thrombosis *

Pathogenesis The changes leading to occlusion of the vein vary somewhat depending upon the etiologic agent In the case of the use of hypertonic or sclerosing solutions or of trauma to the vessel the resulting alterations in the intima are responsible for the initiation of intravascular clotting Spontaneous thrombosis in varicose veins is probably related to the stagnation of blood in such dilated channels Whether or not there is a coexisting low grade bacterial infection in the vicinity of these structures enhancing the thrombotic tendency is still a moot point

Clinical Characteristics

Initial Symptoms and Signs The patient first notices a tender red, and warm area on the extremity which becomes painful on walking or on stretching the inflamed tissues by some other means Physical examination at this time ordinarily reveals a linear area of inflammation about 1 cm (½ inch) wide and of varying length along the course of a superficial vein *(Fig 50) Palpation over the site* discloses an increase in cutaneous temperature and a tender cordlike mass running

* For a complete discussion see *Factors Responsible for Venous Thrombosis* Chap XXIX

in the subcutaneous tissues—the thrombosed vein The process may continue to extend in the vessel or even involve its tributaries but retrograde spread is to some extent prevented by the venous valves The propagation is indicated by the appearance of the inflammatory process in the contiguous skin and of longer segments of occluded vein



FIG 30 Extensive benign thrombophlebitis of superficial veins on posterior surface of left thigh and leg

Late Manifestations If recession occurs the tenderness redness and increased skin temperature gradually disappear generally to be replaced by an outlining linear area of brown pigmentation However the vein may remain as a palpable mass for many weeks afterward in some instances permanently At times the acute process may be replaced by a chronic inflammatory state which results in persistent tenderness in the vicinity of the vessel Fibrotic changes may also take place in the thrombosed segment making the vein much less prominent to palpation On occasion there is recanalization with a re establishment of the local circulation Under such circumstances the cordlike mass disappears entirely and

the only sign to indicate that a superficial thrombosis had occurred is the pigmentation, which may also fade out with time

Complications and Sequelae

Although the common type of superficial thrombophlebitis has been designated as benign this is not always so While the condition is rarely followed by pulmonary embolism, *such a possibility must not be entirely disregarded* This is particularly true if progression of the process takes place in the great saphenous vein with the possibility that the thrombus may pass through the fossa ovalis to reach the femoral vein This may happen in the elderly patient with superficial thrombophlebitis who confines himself to a chair or to the bed in an attempt to lessen the pain associated with movement of the inflamed parts Liberation of pulmonary emboli has also been reported following thrombosis of varicose veins in this type of individual

Superficial benign thrombophlebitis has a tendency to recurrences particularly *if the etiologic agent persists* The change may take place in the same or different vessels Eventually some of the involved areas may show signs of chronic inflammation with the process spreading to the surrounding tissues This produces a site of low grade cellulitis with induration of the overlying skin and tenderness Generally, the thrombosed segment of vein or veins can be palpated running through the mass (For discussion of chronic indurated cellulitis see Chap XVI)

Treatment

Involvement of the Lower Extremity There is some difference of opinion regarding the proper therapy for thrombosis of a previously normal superficial vein of the lower extremity One belief holds that in those instances in which the process is limited to a small portion of the superficial venous system all that is necessary is the application of an Ace bandage to the involved limb This should cover the foot and leg extending some distance proximal to the upper limits of the thrombosed segment The patient may then be ambulatory

If the above procedure does not prevent pain locally on walking the patient is put at bed rest the limb is elevated and hot soaks are applied over the involved site, provided a considerable inflammatory reaction exists This approach is also used if propagation of the process continues and the entire length of the great saphenous vein in the thigh is becoming thrombosed As soon as the local tenderness subsides and signs of inflammation disappear the soaks are discontinued and the patient is allowed to resume his normal activity

It can be argued that placing an individual with an acute superficial thrombophlebitis at bed rest will tend to enhance venous stasis and thus aid thrombosis On the other hand the alternative of physical activity associated with daily chores may theoretically at least also be detrimental on the basis that such a program may predispose to the liberation of emboli Certainly in those cases in which propagation of the process is noted and the thrombus can be felt as high up as the

fossa ovalis * the dangers associated with bed rest are to be preferred to those conceivably following ambulation

Thrombophlebitis occurring spontaneously in varicose veins is treated practically in the same manner as described above In those instances in which recovery is very slow or pain can not be controlled by medical means it may be necessary to excise all or a segment of the great saphenous vein followed by ligation of the divided ends Such a procedure will generally shorten the period of discomfort and disability Ordinarily little difficulty should be expected in postoperative wound healing

Involvement of the Upper Extremity Since in most instances the cause of thrombi is in the upper extremity is the intravenous administration of medications or diagnostic solutions producing injury to the intima the proper approach to therapy is prevention of this type of reaction Precautions should be taken to inject materials which are as isotonic as possible If necessary the patient s blood is withdrawn into the syringe first so as to mix with the drug before the latter is administered In all instances the vein should be penetrated with a minimum of trauma and if repeated venipunctures are required several different sites should be used alternately If despite such measures thrombosis of superficial veins occurs the treatment consists of elevation of the limb on a pillow and the application of hot soaks for several days provided pain is excessive In the presence of minimal symptoms no therapy is indicated

THROMBOPHLEBITIS MIGRANS (IDIOPATHIC RECURRENT SUPERFICIAL MIGRATORY THROMBOPHLEBITIS)

Introduction

Etiology Numerous theories have been advanced to explain the cause of thrombophlebitis migrans but none has been generally accepted Among these suggested causes is infection but positive cultures can only very rarely be obtained from the blood or venous walls and thrombi It has also been proposed that there is a hypercoagulability of the blood perhaps related to an increase in plasma fibrinogen [1] The question always arises as to whether thrombophlebitis migrans is actually a separate entity from the same type of clinical involvement associated with thromboangiitis obliterans (Chap IX) In fact the view has been entertained that it represents a variant of the latter condition in which veins alone are affected [2] In support of this belief is the finding that for the most part the disorder attacks young and middle aged male adults

Pathology Histologically the changes in the vessel wall are inflammatory affecting segments of small and medium sized superficial veins There is marked subintimal fibroblastic infiltration with secondary thrombus formation causing complete obliteration of the lumen The venous wall may be heavily infiltrated with connective tissue which on occasion contains giant cells Little inflammatory reaction is found in the tissues adjacent to the involved vessel nor is there any panniculitis

* Under these circumstances another therapeutic approach is high ligation of the great saphenous vein

the only sign to indicate that a superficial thrombosis had occurred is the pigmentation, which may also fade out with time

Complications and Sequelae

Although the common type of superficial thrombophlebitis has been designated as benign this is not always so While the condition is rarely followed by pulmonary embolism such a possibility must not be entirely disregarded This is particularly true if progression of the process takes place in the great saphenous vein with the possibility that the thrombus may pass through the fossa ovalis to reach the femoral vein This may happen in the elderly patient with superficial thrombophlebitis who confines himself to a chair or to the bed in an attempt to lessen the pain associated with movement of the inflamed parts Liberation of pulmonary emboli has also been reported following thrombosis of varicose veins in this type of individual

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Treatment

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Thrombophlebitis Migrans (Idiopathic Recurrent Superficial Migratory Thrombophlebitis)

Introduction

Etiology Numerous theories have been advanced to explain the cause of thrombophlebitis migrans but none has been generally accepted Among these suggested causes is infection but positive cultures can only very rarely be obtained from the blood or venous walls and thrombi It has also been proposed that there is a hypercoagulability of the blood perhaps related to an increase in plasma fibrinogen[1] The question always arises as to whether thrombophlebitis migrans is actually a separate entity from the same type of clinical involvement associated with thromboangiitis obliterans (Chap IX) In fact the view has been entertained that it represents a variant of the latter condition in which veins alone are affected[1] In support of this belief is the finding that for the most part the disorder attacks young and middle aged male adults

Pathology Histologically the changes in the vessel wall are inflammatory affecting segments of small and medium sized superficial veins There is marked subintimal fibroblastic infiltration with secondary thrombus formation causing complete obliteration of the lumen The venous wall may be heavily infiltrated with connective tissue which on occasion contains giant cells Little inflammatory reaction is found in the tissues adjacent to the involved vessel nor is there any panniculitis

Under these circumstances another therapeutic approach is high ligation of the great saphenous vein

Clinical Characteristics

Thrombophlebitis migrans is characterized by the presence of small red discrete, and tender nodules located on the extremities in the vicinity of superficial veins (Fig 31) Together with the surrounding area of inflammation of the overlying skin, the lesions assume a more linear than circular shape Generally they are

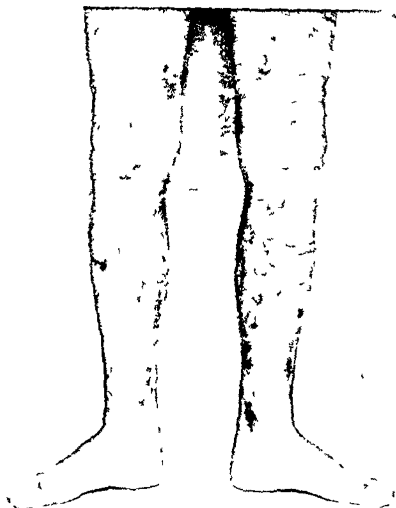


Fig 31 *Thrombophlebitis migrans with involvement of many segments of superficial veins on both lower extremities*

smaller than the nodules of erythema nodosum and erythema induratum although on occasion segments of vein as long as 30 cm (12 inches) may be involved at one time The affected vessel can be felt as a firm indurated cord associated with considerable local rubor The process appears in the form of crops involving segments of a single vein or of different veins in various portions of the extremities While some of the lesions are forming others nearby or even in the same vessel show signs of regression A characteristic of the disorder is the relatively fleeting quality of the nodules most of them lasting for from 7 to 18 days

As the process recedes the cordlike mass becomes less obvious and then may

disappear Frequently, there is a deposit of pigment to mark the site of the previous lesion Necrosis or suppuration of the nodules does not occur

An associated finding in thrombophlebitis migrans may be visceral venous thrombosis This may take place in the intracranial sinuses and in the renal, portal mesenteric and possibly pulmonary veins Rarely involvement of the deep venous system in the extremities may also occur

Treatment

Prophylaxis The treatment of thrombophlebitis migrans for the most part is prophylactic Since there may be some causal relationship between the appearance of this condition and foci of infection if the latter exist proper steps should be taken to eradicate them This applies particularly to diseased tonsils and teeth The use of autogenous vaccines made from bacteria present in the infected material may also be of value As in the case of superficial migratory thrombophlebitis associated with thromboangiitis obliterans abstinence from smoking may prevent a recurrence Anticoagulants have on occasion been used but the results are difficult to evaluate Furthermore, the method is not practicable since the lesions will recur as soon as medication is discontinued

Active Therapy No definitive measures are available for the treatment of thrombotic lesions The patient is advised to be ambulatory and to wear Ace bandages or elastic stockings If the involved segments are so situated that inflamed tissue is stretched with each movement of the leg thus causing pain it may be necessary to prescribe bed rest and elevation of the limb At times hot wet soaks may alleviate the symptoms Whether or not antibiotics should be administered is a moot question When there are concomitant signs of visceral involvement the prolonged and ambulant use of anticoagulants is indicated

Prognosis

The prognosis in thrombophlebitis migrans depends entirely upon whether the process has affected the viscera since under such circumstances death may occur as a result of thrombosis of veins in vital organs If the pathologic change is limited to the vessels of the limbs there is *no mortality* although the condition may be responsible for repeated and prolonged periods of incapacitation

DIFFERENTIAL DIAGNOSIS OF SUPERFICIAL THROMBOPHLEBITIS*

Differentiation of the Two Types of Superficial Thrombophlebitis The distinguishing features between superficial benign [illegible] nbo-phlebitis migrans consist primarily of d[illegible] the veins In the former the thrombosis is [illegible] to a single vein in an extremity and when the process extends it does so by continuity generally in a cephalad direction In the latter there is *no continuity* of spread but instead isolated portions of the same or different vessels are affected at any level No superficial vein in the four extremities appears to be safe from the inflammatory process (For differentiation from deep thrombophlebitis see p 249)

* See also Table 16 p 250

Venous Thrombosis Associated with Thromboangiitis Obliterans Thrombophlebitis migrans must be differentiated from superficial migratory thrombophlebitis associated with thromboangiitis obliterans *Since the appearance of the* lesions and the clinical course are identical, the only basis for distinguishing one from the other is the existence of changes in the arterial system that eventually occur in the case of thromboangiitis obliterans and are never noted in thrombophlebitis migrans, regardless of the duration of the period of observation However, *since superficial migratory thrombophlebitis may be an early manifestation* of thromboangiitis obliterans, at a time when gross impairment in the arteries has not, as yet, occurred *this differential point is not always applicable*

Venous Thrombosis Associated with Malignancy and Infection Another entity which must be excluded before a diagnosis of thrombophlebitis migrans can be made is multiple thrombophlebitis in the extremities associated with carcinoma or infectious diseases particularly tuberculosis and syphilis With regard to malignancy *the approach to the problem involves attempts to determine whether or* not such a lesion exists especially in the body and tail of the pancreas the stomach or the lungs Recurrences of superficial and deep thrombophlebitis of the extremities in an elderly individual, without any apparent reason is very suggestive of this type of condition Confirmatory evidence consists of the finding that large doses of anticoagulants fail to induce a favorable therapeutic response Other differential points are the rapid recurrence of the thrombotic episodes in malignancy and the *short interval intervening between their appearance and the death of the patient*

Cutaneous and Subcutaneous Nodules Thrombophlebitis migrans must also be differentiated from the various clinical entities manifesting nodules in the skin or subcutaneous tissues The significant points in this regard are included in Table 8 p 78 Neoplastic infiltrations such as neurofibroma lymphosarcoma and myosarcoma as well as benign masses like neuroma *should also be considered in* the differential diagnosis In some instances only a biopsy study will reveal the true significance of the nodules

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CHAPTER

XIV VASCULAR DISORDERS AFFECTING THE VENOUS SYSTEM (*Continued*)

2. THROMBOSIS OF DEEP VENOUS SYSTEM

PHLEBOTHROMBOSIS AND NONSUPPURATIVE AND SUPPURATIVE ILIOFEMORAL THROMBOPHLEBITIS

Thrombosis of the deep veins of the lower extremities is a problem of great importance both to the internist and the surgeon. Because of its close association with pulmonary embolism it may alter the entire outlook of a relatively benign illness or an operative procedure. Even if pulmonary embolism does not take place, occlusion of a main venous channel by itself will considerably prolong the post operative course and convalescent period. Furthermore in many instances deep thrombophlebitis leaves the patient with disabling sequelae which may restrict his physical activity for months and even years.

Despite our growing knowledge of the various factors involved in the formation of intravascular clotting and the almost universal acceptance of programs to combat them the incidence of venous thrombosis appears to be on the increase.[4] One suggested reason for this apparent paradox is that our longer span of life permits a greater number of operative procedures on older patients who are generally much more susceptible to intravascular clotting. It is also possible that some of the prophylactic measures on which we rely such as early postoperative ambulation, are not as effective in preventing thrombosis as was originally hoped. (For pathogenesis of venous thrombosis see *Factors Responsible for Intravascular Clotting* Chap XXIX.)

An attempt has been made to divide acute thrombosis of the deep veins of the lower extremities into two types: phlebothrombosis and deep thrombophlebitis (*phlegmasia alba dolens*). This has not met with universal acceptance, since the criticism has been offered that such a differentiation is without physiologic or anatomic basis. Because there is a difference in opinion and because the terms are frequently found in the literature it becomes necessary to evaluate the proposed advantages and the objections to their usage.

MORBID ANATOMY AND PATHOGENESIS

Phlebothrombosis In this state there is considered to be a partial or complete occlusion of the small deep venous plexuses in the muscles of the calf or sole of the foot by a bland thrombus the latter propagates itself without becoming adherent to the wall of the vessel or producing a phlebitis Consequently it becomes jelly like in consistency and friable and is a frequent source of pulmonary emboli Since there is no irritation of the wall stimulation of sympathetic nerves does not occur and hence no vasospastic phenomena are observed Furthermore because the venous channels involved are small at least initially and of little importance in the removal of blood from the extremity there are no clinical signs of venous stasis

Deep Thrombophlebitis In this state the thrombus is located in one of the large deep veins of the lower extremity and is firmly adherent to the vessel due to the resulting inflammatory response in the intima Associated with such changes are a local periphlebitis involvement of the neighboring lymphatic channels in the process and reflex vasospasm Because of the type of reaction in the lumen of the vein the tendency for the liberation of emboli is not very great unless there is propagation of the clot beyond its original site of attachment Since the main venous channels in the limb are occluded there is marked interference with venous outflow producing venous stasis and as a consequence a clinical picture which offers no real diagnostic problem

Disadvantages and Advantages of Classification One of the objections raised to separating deep venous thrombosis into the above described categories is that a bland thrombus in the lumen of a vein will within a period of several hours elicit an intimal inflammatory reaction leading to a phlebitis Second a thrombus originating in the deep venous plexus of the calf and producing no interference with venous return may propagate into the large deep veins of the lower extremity become adherent to the vessel wall and produce all the clinical findings associated with a deep thrombophlebitis Under these circumstances phlebothrombosis can be considered an early phase of deep venous thrombosis with several intermediate stages existing between it and typical deep thrombophlebitis

However the above sequence of events does not always fit the clinical picture For example it is generally agreed that phlebothrombosis can exist followed by pulmonary embolism without the subsequent appearance of thrombosis of large venous channels Conversely a clot may occlude the femoral vein without any previous involvement of the small deep veins in the calf or foot This is particularly true when the process originates in the pelvic veins and then propagates distally a possibility which has recently received clinical support[39]

Therefore on the basis of our present knowledge it would seem reasonable to accept the view that clinically one should differentiate between occlusion of small deep veins of the foot and calf—phlebothrombosis—and a similar process in the large venous channels in the lower extremity—deep thrombophlebitis—although remaining cognizant of the possible errors that might arise because of the close association between the two conditions

CLINICAL CHARACTERISTICS OF PHLEBOTHROMBOSIS

Systemic Reactions

Although an early diagnosis of phlebothrombosis is ordinarily difficult to make there are certain systemic responses generally of a minor degree which may be of help Among these is a slight and simultaneous increase in temperature and pulse and respiratory rates, for which there is no obvious reason, in an individual who has been at complete bed rest for some time or is convalescing from an operative procedure Such findings may be associated with apprehension restlessness, a feeling of impending disaster, and sometimes an ill defined sensation *of something being wrong*[7]

Local Manifestations

Symptoms If together with the above systemic reactions there are some localizing complaints in the lower extremities, the diagnosis of phlebothrombosis is further supported These may consist of an aching or cramplike pain in the *calf at rest with tenderness in this site and in the foot*

Signs Among the local findings in phlebothrombosis are pain in the calf elicited by dorsiflexion of the foot (*positive Homans sign*) tense or spastic calf muscles, the presence of an indefinite mass between the bellies of the gastrocnemius muscle and pain in the lower portion of the leg on passive extension of the foot and plantar flexion of the toes (p 63) Occasionally there may be some findings indicating increased sympathetic tonus, such as cyanosis of the foot, coolness of the skin, and hyperhidrosis Another diagnostic sign is a slight increase in the circumference of the calf determined only by measurement * for obvious edema is generally not present in phlebothrombosis

Laboratory Diagnostic Measures A means of diagnosis of phlebothrombosis which was proposed with much enthusiasm several years ago is venography However it has since been shown that this procedure frequently produces false positive results It is of decisive diagnostic value only if a normal venous pattern has been revealed and thus the absence of venous thrombosis established For the most part the procedure is used only occasionally in phlebothrombosis

Since, despite the application of all the diagnostic procedures already mentioned much too often pulmonary embolism *is still the first sign of venous thrombosis* attempts have been made to devise a laboratory test which would detect incipient thrombosis The early work consisted of a heparin dilution method of determining blood coagulation time[31] Another approach involved *a study of the changes* in the simple (Quick) prothrombin determination[0] Although one can not draw any definite conclusions from the results of such tests it is possible that further research along these lines will be productive in detecting those individuals who tend to develop thrombosis

* Since frequently one calf is normally better developed than the other the determination of the size of the leg at the time phlebothrombosis is suspected is of little value For this reason it should be a routine procedure to obtain such information preoperatively or early in a bed confining illness A fixed reference point *such as the inferior border of the patella* should always be used so that the same site is measured each time

Clinical Characteristics of Acute Nonsuppurative Deep Thrombophlebitis

Systemic Reactions

In contrast to phlebothrombosis constitutional responses in acute deep thrombophlebitis are quite prominent thus contributing significantly to early diagnosis Among these are fever up to 38 9° C (102° F) tachycardia mild malaise leukocytosis and a high sedimentation rate Although the cause of the systemic changes has not been established it is possible that they may in part represent a body reaction to the products of the disintegrated thrombus or a foreign protein like response to the autolysis and absorption of the protein in the edema fluid[4] In any event it is generally accepted that the fever is not the result of infection either in the wall of the vein or in the thrombus itself

Local Manifestations

Symptoms The complaint first noted in the acute stage of deep thrombophlebitis is pain in the involved limb This is located either along the course of the affected vessel and in the groin or in the whole extremity At times the symptom may be very severe Tenderness is generally present in Scarpa s triangle and in the groin and any movement of the limb is associated with a marked exaggeration of the intensity of the complaints

Signs Usually swelling appears soon after the onset of the pain although at times it may occur earlier Depending upon the degree of impairment of local venous return the amount may vary from a barely noticeable pretibial pitting edema to massive involvement of the entire limb (Fig 32) If considerable it may cause the extremity to become brawny and firm due to marked stretching of the superficial structures However as the process recedes the edema becomes pitting in type The leg may appear cyanotic at first but it rapidly becomes white because of compression and collapse of the minute cutaneous vessels by the edema fluid (For a discussion of the factors responsible for the swelling of acute deep thrombophlebitis see *Pathologic Edema* Chap XXVIII)

Suggestive evidence regarding the site of the thrombus can be elicited from a determination of the upper level of the swelling If the involvement is limited to the leg and does not extend beyond the knee then the clot is probably located in the popliteal vein or in the lower portion of the femoral vein However if the thigh is also affected it can be assumed that occlusion of the iliofemoral vein has occurred Associated edema of the scrotum or labia and lower portion of the anterior abdominal wall generally indicates that propagation has taken place into the common iliac vein including the hypogastric branch

If the swelling is first present in one lower extremity and later in the other the possibility must be considered of extension up into the inferior vena cava with involvement of the opposite iliac vein Of course such a clinical picture might also result from a simultaneous but unrelated thrombosis in the iliofemoral vein of both extremities In each instance progression of the disease process is heralded

by the spread of the swelling to a higher level and an increase in pain which also extends upward

Among other important findings in the acute stage of deep thrombophlebitis are prominence and distension of the superficial veins due to the increased venous pressure Such changes generally indicate either thrombosis above the level of the femoral vein, placing the major burden of venous drainage on the great saphenous

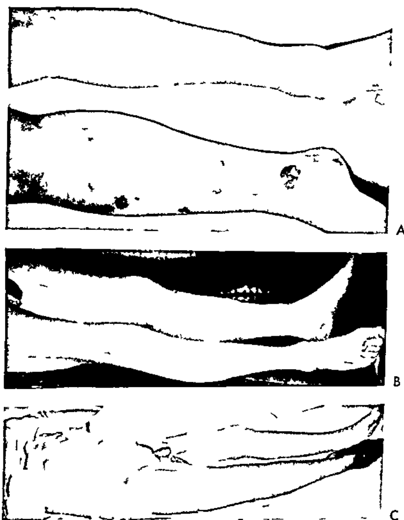


Fig 32 Acute deep iliofemoral thrombophlebitis A Marked swelling of right leg and thigh with some superficial ulceration B Swelling of left leg and thigh C Phlegmasia cerulea dolens with bullae and gangrene of foot

vein and its tributaries or occlusion of the mouth of the great saphenous vein increasing the pressure in the superficial venous system It must be pointed out however, that the distension of the superficial vessels may not readily be discernible because of the masking effect of the edema

Later Manifestations

As the acute stage of deep thrombophlebitis subsides pain and swelling become less and finally disappear It is of interest that tenderness in Scarpa s triangle may

persist for some time after other findings have gone With disappearance of local signs and symptoms the pulse rate, white blood count and sedimentation rate also tend to return to normal If with the initiation of an ambulation program there is a recurrence of pain or swelling this indicates that activity has been begun prematurely and that a more protracted period of bed rest is required

Complications of the Acute Stage

Acute Peripheral Circulatory Failure Rarely acute deep thrombophlebitis is associated with such massive edema in the involved limb that the patient may go into a state of shock due to loss of circulating blood volume This is more likely if both lower extremities are affected by the thrombotic process Aside from the local changes the clinical picture will resemble that ordinarily observed in oligemic shock and the treatment is likewise the same

Pulmonary Embolism Although a relatively infrequent complication a piece of the clot may be liberated to enter the blood stream and lodge in the pulmonary bed This occurs if the thrombus has propagated above the original site of phlebitis

Nutritional Disturbances On occasion trophic changes may appear in the acute stage of deep thrombophlebitis despite the existence of a previously normal arterial circulation Such complications are noted in the type designated as phlegmasia cerulea dolens or blue thrombophlebitis [9, 1] characterized by a massive involvement of the venous circulation In this state the pain is usually excruciating first being located in the calf or groin but eventually involving the whole limb The skin assumes a deeply violaceous or cyanotic hue with purpuric areas or petechiae like lesions scattered over the extremity The swelling is generally quite marked and may be responsible for the frequent appearance of cutaneous blebs and even bullae (Fig 32C) Pulsations in the arteries locally become diminished and may disappear and there is a reduction in cutaneous temperature of the limb In some instances gangrene of toes or part of the foot and even leg may occur

The pathogenesis of phlegmasia cerulea dolens is not clear although several factors have been implicated There appears to be little question that obstruction of venous return in an extremity provided it is of sufficient extent can cause a great reduction in arterial inflow Whether the responsible mechanism is wholly the occlusion of the minute vessels by the pressure of the edema fluid or whether the rapidity with which this takes place also plays a role is difficult to state Another mechanism which has been implicated is the associated vasospasm which tends to aggravate the ischemic process

Clinical Characteristics of Suppurative Deep Thrombophlebitis

In suppurative deep thrombophlebitis the thrombus occluding a main deep venous channel of the lower extremity is infected This may result from auto infection of the clot present in nonsuppurative deep thrombophlebitis from an injury to the limb or from retrograde propagation of a suppurative pelvic thrombophlebitis into the iliofemoral vein The latter possibility may follow postabortal or postpartum infection pelvic abscesses gynecologic operations or the intra uterine application of radium

by the spread of the swelling to a higher level and an increase in pain which also extends upward

Among other important findings in the acute stage of deep thrombophlebitis are prominence and distension of the superficial veins due to the increased venous pressure Such changes generally indicate either thrombosis above the level of the femoral vein, placing the major burden of venous drainage on the great saphenous

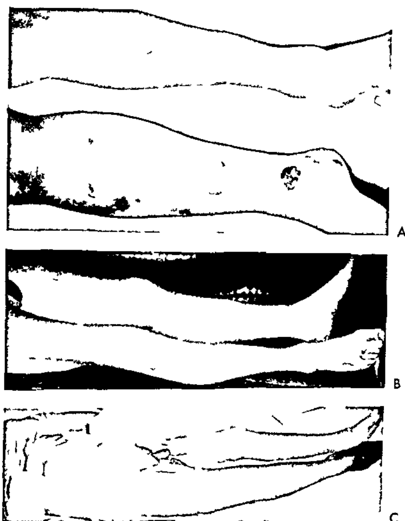


Fig 32 Acute deep iliofemoral thrombophlebitis A Marked swelling of right leg and thigh with some superficial ulceration B Swelling of left leg and thigh C Phlegmasia cerulea dolens with bullae and gangrene of foot

vein and its tributaries or occlusion of the mouth of the great saphenous vein increasing the pressure in the superficial venous system It must be pointed out however, that the distension of the superficial vessels may not readily be discernible because of the masking effect of the edema

Later Manifestations

As the acute stage of deep thrombophlebitis subsides pain and swelling become less and finally disappear It is of interest that tenderness in Scarpa's triangle may

them being acute arterial occlusion posttraumatic vasomotor disturbances acute cellulitis and superficial thrombophlebitis (For a discussion of distinguishing points of acute arterial occlusion see *Differential Diagnosis of Arterial Occlusion* Chap XX)

Since vasospasm and swelling are frequently noted in posttraumatic vasomotor disorders this condition must also be differentiated from acute deep thrombophlebitis The close relationship between an injury to a joint or to other tissues of a limb and the appearance of clinical findings is of value here At the same time there is no history of an acute onset of marked swelling affecting most of the extremity nor are there any signs indicating the presence of a block in the main venous channels Determination of walking venous pressure measurements in the lower extremity may also be of diagnostic importance (For discussion of this point see *Venous Pressure Measurements in the Lower Extremities* Chap XXV)

Several findings should help differentiate nonsuppurative deep thrombophlebitis from acute cellulitis of the tissues of the lower extremity In the latter the systemic response is generally greater although not as marked as in suppurative deep thrombophlebitis Swelling is also present in acute cellulitis but it frequently is nonpitting in type and limited to the area of inflammation without encompassing the entire circumference of the limb at any one level This is in contrast with the usually pitting, uniform edema involving the entire leg or leg and thigh noted in deep thrombophlebitis Associated with the swelling there are other signs of inflammation in acute cellulitis such as local rubor and elevated skin temperature bounding pulses lymphangitis and regional lymphadenitis In comparison in deep thrombophlebitis there may be findings due to vasospasm such as pallor or cyanosis of the skin a low cutaneous temperature hyperhidrosis and reduced arterial pulsations

Little difficulty should be encountered distinguishing acute superficial thrombophlebitis from acute deep thrombophlebitis Involvement of the superficial veins is generally associated with no change in body temperature white blood count and sedimentation rate while in deep thrombophlebitis these readings are almost invariably increased Locally the clinical picture is also entirely different In every case of superficial thrombophlebitis signs of inflammation are present in the vicinity of the involved vein and the skin overlying the vessel is warmer than normal This response outlines the course and length of the affected segment The vein itself can be felt as a firm tender mass under the skin No uniform pitting edema of the leg or thigh is noted although there may be some swelling in the neighborhood of the thrombosed vein On the other hand edema of the leg and foot is practically always found in deep thrombophlebitis while the superficial veins are normal in appearance except for some fullness Nor does the skin over the vessels demonstrate any signs of inflammation

TREATMENT

PROPHYLACTIC MEASURES

The logical approach to the control of deep venous thrombosis is to prevent its inception This should be carried out in every patient whether medical or

Systemic Reactions

The constitutional responses are much more severe than in nonsuppurative deep thrombophlebitis The onset is generally heralded by chills a high spiking relapsing fever, and other signs of a serious blood borne infection The pulse is rapid, remaining so in the face of wide ranges of temperature and the same change is noted in the respiratory rate, even when pulmonary involvement is not present

Local Manifestations

The localizing findings in the involved extremity are similar to those observed with nonsuppurative deep thrombophlebitis, although usually the pain in the region of the thrombus is more marked because of the greater degree of associated inflammatory reaction In the female, if the origin of the condition is in the pelvic veins vaginal examination may reveal hard tender cords in the base of the broad ligament or thrombosed veins leading from an infected operative site Frequently such a procedure is followed by a definite rise in body temperature within 24 hours a finding which can be used as a diagnostic sign

Differential Diagnosis

Phlebothrombosis

As has already been stressed the acute phase of phlebothrombosis is associated with only minor local changes and mild constitutional reactions Therefore its differential diagnosis from other states or conditions affecting the tissues comprising the calf presents a real problem For example a patient whose leg or foot had been resting in a stirrup during the entire course of a surgical procedure subsequently might well have complaints referable to the limb especially if the irritated tissues are placed on stretch as in the course of eliciting the Homans sign The same situation may arise if the individual allows the full weight of his leg to rest on the calf for a protracted period while recovering from the effects of the anesthetic Other conditions which may produce symptoms in the back of the leg (and hence mimic a positive Homans sign) are superficial thrombophlebitis chronic and acute cellulitis dermatitis a shortened Achilles tendon, myofibrositis, local hemorrhage and laceration and contusion of muscles

It would seem therefore that pain in the calf both at rest or with movement, and even a positive Homans sign are not sufficient evidence on which to base a diagnosis of phlebothrombosis unless all other mechanisms which simulate such a clinical picture are first excluded Unfortunately even then one may not be entirely certain of the diagnosis until it is confirmed by the appearance of signs indicating that pulmonary infarction has occurred

Deep Thrombophlebitis*

Because of the obvious localizing findings and the associated systemic responses the acute stage of deep thrombophlebitis is readily identified However on occasion a number of conditions may mimic some of its clinical aspects among

* See Table 16

Table 16 (continued)

	Acute nonsuppurative iliofemoral thrombophlebitis	*Phlebothrombosis*	*Superficial benign thrombophlebitis*	*Acute cellulitis with lymphangitis*	*Acute arterial occlusion of main artery*
Color of skin	Cyanosis *due* to vasospasm or pallor from stretching of skin by *edema*	On occasion *cyanosis* due to slight vasospasm	Rubor over inflamed vein	Rubor over entire lesion and surrounding tissue	Marked pallor due to impairment of arterial inflow and vasospasm mottled cyanosis
Homans *sign*	Generally not present unless calf veins are also involved	*Usually present*	Not present but a false positive test may be *elicited* if lesion is near calf	Not present but a false positive test may be elicited if lesion is located over calf	Not present but a false positive test may be elicited if occlusion has occurred at bifurcation of popliteal artery
Pulmonary embolism	Relatively infrequent *complication*	Relatively *frequent* complication	*Very rare* complication	Never present	Never present
Peripheral arterial *pulsations*	Normal but difficult to palpate because of edema at times may be *reduced due to* vasospasm	Normal	Normal	May be bounding because of vasodilatation	Invariably absent because of occlusion of main artery and associated vasospasm
Trophic changes	*Rarely gangrene* of a toe in very severe case or if there is coexisting arterial *impairment*	Not present	Not present	Not present	Gangrene of toes or of rest of foot *frequently* present
Neurologic findings	Inability *to* dorsiflex foot because of edema no real neurologic findings	Not present	Not present	Not present	Stocking-glove type of anesthesia or hypesthesia foot drop inability to move toes numbness of toes

Table 16 Differential Diagnosis of Acute Deep Thrombophlebitis of Lower Extremity

	Acute nonsuppurative iliofemoral thrombophlebitis	*Phlebothrombosis*	*Superficial benign thrombophlebitis*	*Acute cellulitis with lymphangitis*	*Acute arterial occlusion of main artery*
Type of onset systemic reactions	Acute Increased sed rate leukocytosis fever up to 38 8°C (102°F) malaise increase in pulse rate rarely chills	Insidious Slight increase in temp respiration pulse rate no leukocytosis or increased sed rate	Acute Generally no systemic reactions	Acute Increase in sed rate leukocytosis fever up to 40 0°C (104°F) moderate malaise chills tachycardia	Acute Generally no systemic reactions during acute phase
Pain and tenderness	In Scarpa s triangle and in groin and along course of femoral vein pain also present in leg and foot	No pain but tenderness deep in calf and in plantar portion of foot	No spontaneous pain but tenderness along course of involved vein pain on stretching of inflamed tissues as by walking	Pain in area of inflammation tenderness in same site and in surrounding tissues pain on stretching tissues	Severe excruciating pain in toes and rest of foot and pain and tenderness over occluded portion of artery
Swelling	Marked uniform involving entire circumference of leg or whole limb pitting if skin is not stretched too tightly by fluid	Not apparent except by measurement	None present except possibly locally over lesion	Local swelling over lesion nonpitting	None limb is smaller if anything
Skin temperature	Normal increased or decreased	Normal or possibly slightly decreased	Increased in vicinity of lesion normal elsewhere in limb	Increased in vicinity of lesion	Marked decrease in foot leg and even lower thigh at times
State of superficial veins and venous pressure	Veins distended and prominent unless masked by edema venous pres high	Veins normal or slightly distended venous pres normal	Involved vessels cord-like due to thrombosis others normal venous pres normal	Veins normal venous pres normal	Veins collapsed venous pres decreased

and older who have undergone an operative procedure or are bedridden [32] Immediately after surgery the bandages are placed around the lower extremity beginning with the toes and extending upward to the groin In this manner stagnation of blood in the superficial veins is obviated and at the same time shunting occurs into the deep vessels with an acceleration of flow The desired effect is enhanced by elevating the foot of the bed by 10 inches thus utilizing gravity to advantage

Early ambulation may likewise contribute to the prevention of venous stasis [18] Theoretically at least the shorter the period during which the latter state exists, the less should the tendency be for venous thrombosis

Prophylaxis During and After Surgery

Care should be taken during surgery to minimize trauma to tissues since such a response may be followed by changes in the blood plasma which predispose to increased coagulability Special precautions must likewise be observed to protect the veins in the vicinity of the operative field for otherwise changes in the intima of these vessels may occur and consequently thrombosis Knee crutches and leg holders should be well padded and a restraining strap if used should not be tight Attempts should also be made to counteract the increased viscosity of the blood which generally results postoperatively from dehydration following loss of fluid and electrolytes

Treatment of Potential Candidates for Venous Thrombosis

Medical Therapy Since individuals who have had one or more attacks of intravascular clotting have a greater tendency than normal persons to develop similar episodes when placed at complete bed rest the program of prophylaxis utilized for them is necessarily more carefully controlled and intensified This approach is also applicable to patients who are potential subjects for venous thrombosis because of either widespread tissue trauma marked venous stasis due to impaired cardiac function or extensive pelvic surgery particularly for abdominal malignancy Besides the measures already mentioned of great importance in the prevention of intravascular clotting in this group of subjects is the institution of a course of slow-acting anticoagulant therapy for the entire period of bed-confinement and the first week of ambulation (For administration of anticoagulants see Chap XXIX)

When dicumarol is given postoperatively certain precautions must be taken Since there is a possibility of bleeding from the operative site administration of the drug is delayed for or 3 days so that the therapeutic level which generally takes 36 to 7 hours to be reached is established 4 or 5 days following operation Even under these circumstances one must still be on the alert for the appearance of postoperative bleeding especially between the sixth and tenth day of therapy

Surgical Therapy In recent years ligation of both femoral veins below the junction of the deep femoral vein has had an extensive clinical trial for the prevention of pulmonary embolism in individuals with a tendency to intravascular clotting This has been especially true in the case of elderly candidates for surgical

surgical, who is required to remain at complete bed rest for any period of time The aim of such a plan is to eliminate or at least reduce the potency of those factors which are conducive to intravascular clotting particularly venous stasis (Chap XXIX)

Steps to Eliminate or Reduce Venous Stasis

Since the greatest single factor favoring venous stasis of the lower extremities is physical inactivity frequent planned and supervised voluntary movements of the legs should be carried out during the entire period of bed confinement The regimen should include active flexion and extension of the feet, legs, and thighs and movement of the feet against some type of resistance

The use of an electrically operated apparatus has also been advocated to cause passive muscular contractions of the muscles of the thigh and calf induced by a sinusoidal current [illegible] The procedure is begun as soon after operation as possible since thromboses of deep veins have been reported to occur within 3 days after the beginning of a period of confinement [14] Such a measure is useful during the first or second postoperative days, at a time when it is difficult to persuade the patient to make voluntary movements because of the fear of initiating pain in the operative site Later more strenuous exercise, such as the use of the bed bicycle, may be worthwhile [11] All the procedures should be carefully supervised by the nursing staff

Precautions should likewise be taken to avoid obstruction to venous return The use of pillows under the knees is contraindicated, since this enhances the normal interference to the movement of blood out of the limb resulting from the anatomic relationship of the structures in the popliteal space Placing the patient in Fowler s position and applying tight abdominal dressings should be avoided for such measures reduce venous outflow by raising intra abdominal pressure At the same time abdominal binders restrict the motion of the diaphragm which also contributes to venous stasis

Repeated deep breathing helps reduce venous stasis in the legs since it increases venous return from these sites the mechanism being an exaggeration of the one operating with normal inspiration (p 472) Therefore as soon as the surgical patient regains consciousness he should be instructed to take 12 to 15 deep breaths every hour during the day In this regard it is necessary to limit the use of sedatives for otherwise there may be some depression of respiration

Since a certain amount of vasoconstriction of the peripheral vessels is generally associated with the immediate postoperative period it is advisable to counteract such a tendency This is accomplished by the application of heating pads or diathermy to the abdomen to produce indirect vasodilatation in the extremities or by direct warming using a thermostatically controlled heat cradle This will cause an increased rate of blood flow through the arterioles and capillaries and hence through the venous bed The more rapid circulation will facilitate the return of blood to the heart and thus prevent venous pooling

The routine use of compression bandages applied to the lower extremities has also been advocated as a prophylactic measure in individuals 45 years of age

and older who have undergone an operative procedure or are bedridden[7,8] Immediately after surgery the bandages are placed around the lower extremity beginning with the toes and extending upward to the groin In this manner stagnation of blood in the superficial veins is obviated and at the same time shunting occurs into the deep vessels with an acceleration of flow The desired effect is enhanced by elevating the foot of the bed by 10 inches thus utilizing gravity to advantage

Early ambulation may likewise contribute to the prevention of venous stasis[14] Theoretically at least the shorter the period during which the latter state exists the less should the tendency be for venous thrombosis

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Care should be taken during surgery to minimize trauma to tissues since such a response may be followed by changes in the blood plasma which predispose to increased coagulability Special precautions must likewise be observed to protect *the veins in the vicinity of the operative field* for otherwise changes in the intima of these vessels may occur and consequently thrombosis Knee crutches and leg holders *should be well padded and a restraining strap if used should not be tight* Attempts should also be made to counteract the increased viscosity of the blood which generally results postoperatively from dehydration following loss of fluid and electrolytes

Treatment of Potential Candidates for Venous Thrombosis

Medical Therapy Since individuals who *have had* one or more attacks of intravascular clotting have a greater tendency than normal persons to develop similar episodes when placed *at complete* bed rest the program of prophylaxis utilized for them is necessarily *more carefully* controlled and intensified This approach is also applicable to patients who are potential subjects for venous thrombosis because of either *widespread* tissue trauma, marked venous stasis due to impaired cardiac function *or extensive* pelvic surgery particularly for abdominal malignancy Besides the measures already mentioned of great importance in the prevention of intravascular clotting *in* this group of subjects is the institution of a course of slow acting anticoagulant *therapy* for the entire period of bed-confinement and the first week of ambulation (For administration of anticoagulants see Chap XXIX)

When dicumarol is given postoperatively *certain* precautions must be taken Since there is a possibility of bleeding from the operative site administration *of the* drug is delayed for 2 or 3 days so that the therapeutic level which generally takes 36 to 72 hours to be reached is established 4 or 5 days following operation Even under these circumstances one must still be on the alert for the appearance of postoperative bleeding especially between the sixth and tenth day of therapy

Surgical Therapy In recent years ligation of both femoral veins below the junction of the deep femoral vein has had an extensive clinical trial for the prevention of pulmonary embolism in individuals with a tendency to intravascular clotting This has been especially true in the case of elderly candidates for surgical

procedures. However, the original enthusiastic advocacy of such an approach has been considerably dampened by the appearance of many unfavorable reports. Even the original supporters of the measure now admit that it is no more effective than anticoagulant therapy in the prevention of pulmonary embolism.[8] Others have gone even further and have stated on purely theoretical grounds that the operation does not appear to be basically sound.[19] However, when contraindications to the use of anticoagulants exist (pp. 480 and 484), then the only recourse left in the case of the potential candidate for venous thrombosis is vein ligation.

THERAPY IN DEEP VENOUS THROMBOSIS

Once the diagnosis of deep venous thrombosis in the lower extremity has been made, the therapeutic approach will depend upon the type of pathologic process that exists.

Phlebothrombosis

Since the diagnosis of phlebothrombosis is only infrequently made before pulmonary embolism occurs, its treatment for the most part resolves itself into therapeutic attack upon its main complication as well as steps to prevent further such episodes. The condition locally produces no disabling sequelae unless propagation of the thrombus causes occlusion of main venous channels. The first approach to the problem therefore is the prevention of the condition by means of the various procedures already enumerated in this chapter. If one is fortunate to make a diagnosis of phlebothrombosis before the appearance of embolic phenomena, then a definite program should immediately be set up. This consists of the institution of anticoagulant therapy, using both heparin and dicumarol, and/or bilateral femoral vein ligation below the junction with the deep femoral vein. *The pros and cons of the latter procedure are discussed in connection* with the treatment of pulmonary embolism (Chap. XV).

Acute Nonsuppurative Deep Thrombophlebitis

Control of Venous Stasis. The first step is to place the patient at complete bed rest and elevate the foot of the bed so that the toes are at a higher level than any other part of the body. In the hospital this can be accomplished by *cranking up the distal half of the bed to form a 45 degree angle* with the proximal portion. Care should also be taken to maintain the lower extremity extended rather than flexed at the knee in order to facilitate venous return through the popliteal space. At the same time acute flexion of the hips should be avoided.

Removal of Vasospasm. *This can be accomplished through the application of* local heat using a thermostatically controlled cradle. The limb is wrapped in large moist towels from the groin to the toes and the surrounding temperature is maintained around 35° C. (95° F.). Not only does this procedure inhibit excessive vasomotor tonus and *thus increase blood flow* but *it also tends to* counteract the periphlebitis. It is generally utilized for at least the first week during the period when the pain and swelling are marked.* Another means which

* In those occasional instances in which the application of heat causes an accentuation of symptoms, cold packs should be substituted.

has been suggested for removal of vasospasm is the use of daily paravertebral lumbar sympathetic blocks with procaine [3] However since the patient is generally on anticoagulants (see below) and since under these circumstances there is a definite risk associated with the procedure (p 446) for the most part blocking of the paravertebral sympathetic ganglia has only a limited application in the acute stage of deep thrombophlebitis The measure falls into the category of symptomatic treatment causing a reduction in pain and swelling [6] but does not appear to have any permanent influence upon the subsequent course of the disease or its sequelae

Control of Pain Since most patients complain of severe pain during the initial period of the thrombophlebitis the temporary use of narcotics such as codeine or morphine becomes almost a routine measure At the beginning frequent administration may be necessary to control the complaints Because of the possibility that vasospasm may in part be responsible for the pain it is worthwhile to utilize one of the sympathetic blocking agents as adjunct therapy Of value in this regard are Priscoline 25 mg orally 3 times a day or 50–75 mg intramuscularly or Hydergine 0 3 mg intramuscularly

Prevention of Dislodgment of Clots Although periodic deep breathing may help prevent venous thrombosis and pulmonary embolism in the patient at complete bed rest once these conditions exist such a program is definitely contraindicated Deep breathing as already mentioned alters the gradient of external pressure to which the inferior vena cava is exposed in its course and thus accelerates the rate of blood flow upward into the heart To some extent this action manifests itself as a *suction effect* which in the presence of a loosely attached thrombus or one with a long tail projecting into the lumen of a main vein may cause a portion to break off to produce a pulmonary embolism Therefore, when intravascular clotting is present even the common practice of having the patient breathe deeply or cough during the course of a physical examination of the chest should be dispensed with If there is some question as to the presence of a pulmonary infarction reliance should be placed on x ray examination rather than the elicitation of abnormal physical findings in the lungs

Anticoagulants As soon as the diagnosis of deep thrombophlebitis is made anticoagulants should be started Since an immediate effect is desired heparin should be used in conjunction with dicumarol the exact technic of administration of both drugs being described in Chapte XXIX When the prothrombin activity of the blood has been depressed to the desired level (prothrombin determination of 20 per cent Quick curve) heparin is discontinued and the patient is maintained on dicumarol until he becomes completely ambulatory

Several situations require special precautions in the administration of anticoagulants or even their elimination as a therapeutic tool One of these is the postoperative development of deep thrombophlebitis Because of the possibility of bleeding from the operative site many surgeons hesitate to use such medications However the danger i generally minimal [illegible] us thrombosis in most instances [illegible]

[illegible] time sufficient reparative

[illegible] significant hemorrhage

[illegible] of anticoagulant therapy in deep venous thrombosis associated with pregnancy has not been fully answered Although the parturient mother

may be more resistant to the effects of anticoagulants than a nonpregnant subject this is not true for the fetus or the newborn In fact, the prothrombin level of the infant has been found to be significantly lower than normal Since dicumarol passes across the placental barrier to the fetus the possibility—supported by experimental evidence—of the drug causing a hemorrhagic tendency in the latter must be considered[1, 7] On the other hand certain clinical studies suggest that dicumarol properly administered can be safely used antepartum[1, 1] Because of such contradictory evidence, it would seem advisable to utilize anticoagulants in the pregnant state only when the indications are unequivocal At the same time the patient and her family should be made aware of the possibility of untoward effects on the baby

In the case of venous thrombosis occurring in the postpartum period anticoagulants have had limited trial as treatment because of the reluctance of physicians to administer them in the presence of vaginal bleeding However there is little evidence in favor of this point of view Clinical studies have not revealed the appearance of complications following such therapy[8] nor has there been any increase in postpartum vaginal bleeding[6] It is the general belief however that anticoagulants should not be given before the eighth postpartum day and then only if the uterus is normally involuting Since a small amount of dicumarol appears in the milk of lactating animals on this medication,[10] the advisability of weaning infants from dicumarilized mothers seems obvious In all instances in which anticoagulants are administered but particularly in the situations described above it is of greatest importance that careful laboratory control should be maintained and that the physician should be continuously on guard for the first signs of abnormal bleeding

Rehabilitation Program With the disappearance of the edema and the subsidence of all signs of active infection typified by a fall of the sedimentation rate to normal, the patient is placed on a routine of exercises in bed preparatory to ambulation First he is encouraged to move his toes provided this does not cause too much discomfort and then the degree of physical activity is gradually increased during the period of bed rest That such a procedure may result in the dislodgment of a portion of the thrombus followed by a pulmonary embolism is a theoretical possibility, but this has not been substantiated by clinical evidence

Having provided the patient with a well fitting elastic stocking in order to prevent the recurrence of swelling the ambulation program is begun If, despite this aid there is a return of edema it can be assumed that a longer period of bed rest is necessary in order to allow for the formation of a more efficient collateral circulation The only way to determine when this exists is to expose the patient to trial periods of ambulation followed by measurements of the circumference of the limb to note whether or not swelling has occurred When the edema appears to be controlled with the use of an elastic stocking normal activity is gradually re-established

The above regimen can be modified somewhat by the use of a compression bandage early in the acute stage The desired effect is obtained with a #8 Ace bandage applied to the extremity from the toes to a point beyond the upper extent of the edema When the thigh is also involved, it is advisable to use two separate

bandages one for the foot and leg and the other for the thigh leaving the knee free If the bandage is wound too tightly it will cause severe pain while a loosely applied one will not produce any alleviation of symptoms With a reduction in edema the elastic band should be rewrapped again using adequate tension The advantage of the compression bandage is that the patient can become ambulatory soon after the acute phlebitis shows signs of subsiding thus decreasing the necessary period of complete bed rest and hospital stay

Some times the patient with acute deep thrombophlebitis is subjected to an unnecessarily long period of confinement in bed with the result that the signs of disuse overshadow the findings of the original disorder Under these circumstances a program of physical therapy must be set up which encourages the patient to bear weight on his foot first with the aid of crutches then with a cane and finally without any supports At the same time active and passive motion to the involved foot is intensively applied so as to counteract the partial ankylosis and the atrophy and poor tonus of muscles which invariably follow disuse Correct posture and a normal gait should also be emphasized

In summary treatment of acute nonsuppurative deep thrombophlebitis consists of bed rest elevation of the involved limb and the use of anticoagulants Of value also is removal of vasospasm which generally results in a reduction of swelling and pain In the uncomplicated case such a program of therapy should result in the disappearance of the clinical findings within several weeks

Acute Suppurative Deep Thrombophlebitis

When the thrombus in the main venous channel is infected intensive treatment is necessary for otherwise sepsis and fatal pulmonary embolism are likely to occur Of prime importance is immediate ligation of the affected vein above the level of thrombosis In the case of involvement of pelvic veins the inferior vena cava and both sets of ovarian vessels may have to be tied off The surgical procedure should be supplemented by large doses of appropriate antibiotics Once the infection is controlled future therapy is similar to that outlined in the preceding section

Prognosis and Sequelae

Phlebothrombosis [illegible] infarction then an un[illegible] of sequelae occur as a res[illegible] the primary lesion since the veins that are involved are of minor importance in the removal of blood from the lower extremity

Nonsuppurative Deep Thrombophlebitis In the acute stage of this disorder the relatively infrequent complications largely determine prognosis Obviously the liberation of a thrombus and its lodgment in the pulmonary vascular bed will make the outlook much more serious The same is true for the appearance of a state of shock Phlegmasia cerulea dolens may result in gangrene of sufficient extent to necessitate amputation of a limb while the same situation may arise if deep thrombophlebitis of a moderate degree affects an extremity with an impaired arterial circulation

In the uncomplicated case the outlook depends upon the efficiency of the newly formed collateral venous system and upon the changes that occur in the thrombosed segment of vein. The rate of formation of collateral vessels appears to some extent to be related to the efficacy of the early treatment. If adequate anticoagulant therapy is carried out, the possibility of propagation of the thrombus into larger veins or into tributaries of the original vessel is minimized. Hence more patent channels are available for the removal of blood from the extremity, now that the main vein is blocked. Furthermore, if ambulation is delayed until this collateral circulation is effective and if elastic stockings are subsequently used to control the swelling, the possibility of reducing or even eliminating sequelae is enhanced. If, however, no precautions are taken in this regard, the patient may be partly or completely disabled for some time after the acute process has subsided.

In some instances, despite diligence, extensive thrombosis of the main venous channel and its tributaries will cause marked impairment in venous outflow. If the thrombosed segment of vein should later become recanalized, the situation is not bettered, since the local valves are generally destroyed in the process. Such a change is followed by a backward flow in the entire length of the venous channel on the assumption of the upright position, and as a consequence a further aggravation of the existing venous stasis. As a result of the prolonged maintenance of the latter state, the patient may develop certain sequelae, which although less dramatic than the early findings, are nevertheless disabling. Such changes have been termed the "postphlebitic syndrome" and include edema, dilated and varicose veins, stasis dermatitis, pigmentation, chronic indurated cellulitis, and ulceration. A discussion of these alterations and their treatment is presented in Chapter XVI.

Suppurative Deep Thrombophlebitis. The outlook in this condition is poor. If embolic phenomena have not been prevented, then multiple lung abscesses will form. The local process in the vein may spread and cause widespread thrombosis of the pelvic veins.

PRIMARY THROMBOSIS OF AXILLARY AND SUBCLAVIAN VEINS

General Considerations

The appearance of a more or less acute venous obstruction in the upper extremity of an otherwise healthy person has been designated as a clinical entity and given a number of different names, among them primary or effort thrombosis of the axillary and subclavian veins, so-called traumatic thrombosis, intermittent venous claudication, and finally, Paget-Schroetter's syndrome, after the first two workers to describe it as a specific disorder.[13] The most commonly used term is primary thrombosis of the axillary and subclavian veins.

Etiology. The exact cause of the condition is not known, although several etiologic agents have been proposed, among them trauma to the intima of the vein. In favor of such a view is the finding that frequently just preceding the onset of the disorder the patient had indulged in some type of exercise which produced a muscular strain, such as swinging at a golf ball, doing setting-up exercises, or pitching a baseball. At times there is a history of some unusual violent muscular

effort It has also been suggested that injury to the axillary vein may occur in the course of daily activity as a result of compression of the vessel between the head of the abducted humerus and the subclavius muscle [8] Another possibility is that in certain individuals with high horizontally curving first ribs and upward and backward directed clavicles a backward thrust of the shoulder girdle may increase compression of the subclavian vein which on occasion will lead to thrombosis Aside from strain or trauma spasm of the subclavian vein has been mentioned as an etiologic factor On this basis it has been postulated that the response is secondary to pressure on the vessel either by the subclavius muscle tendon the scalenus anticus muscle or a combination of both [18]

Incidence Although the disorder may occur at practically any age and in both sexes it is predominantly noted in active robust males between 20 and 40 years of age with well developed neck and shoulder muscles The right arm is involved more often than the left In some instances when the left axillary vein is occluded either the patient is found to be left handed or a history may be elicited of the left upper extremity having been subjected to an unusual strain

CLINICAL CHARACTERISTICS

Systemic Reactions

Rarely is the acute phase of the disease associated with any systemic disturbances The temperature and pulse are generally normal while only occasionally is there an increase in leukocytes or a prolongation of the sedimentation rate These changes are in contrast with those observed after thrombosis of the main venous channel in the lower extremity

Local Manifestations

Symptoms The onset of complaints is usually acute At first there is an initial sense of tightness and fullness of the involved extremity and a dull generalized aching in the shoulder or arm which then extends down into the hand The limb feels heavy and stiff Rarely is there severe pain and in some instances there may be none When propagation occurs in the course of the brachial vein pain may be experienced along the inner aspect of the arm There may be weakness and numbness of the extremity which may progress to the point where the patient is unable to move it

Sign Swelling is invariably present It may either begin so insidiously that it is unnoticed by the patient until it becomes quite prominent or its onset may be sudden the whole extremity from fingertips to shoulder manifesting massive edema within several hours after the pain is first experienced The process may also extend onto the chest wall and into the neck In some cases the swelling can not be pitted even when considerable in amount probably because a part of the increase in size of the limb is due to distension of the veins However, in others an actual increase in tissue fluid is the chief factor thus resulting in a soft and compressible type of edema That a high venous pressure exists is supported by the consistent findings of prominent cubital veins which fail to collapse on elevation of the limb and venous pressure readings of 300 mm water or more particularly

after exercise [79] Palpation in the axilla may reveal the presence of a cordlike thrombosed axillary vein

Soon after the swelling decreases, the collateral venous circulation becomes more obvious this occurring within a few days to several weeks after the onset of the condition The vessels remain prominent for many years and perhaps for

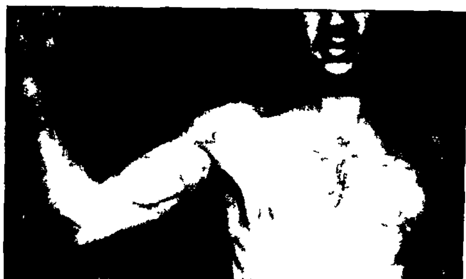




FIG 33 Right axillary vein thrombosis A Demonstration of superficial venous network on arm and chest wall made more apparent with the use of infrared photography B Collateral vessels in same patient visualized by means of venography

ever unless recanalization takes place in the thrombosed segment of axillary or subclavian vein The ramifications of the collateral vessels in the arm axilla and chest wall can be readily outlined by either infrared photography or venography (Fig 33) The latter procedure may also be of value in localizing the site of occlusion, but it is of little use in determining either the extent or cause of the

process (For anatomy of newly formed collateral circulation, see *Venous Collateral Networks* Chap XXVI)

The involvement of the arterial tree in the disorder consists chiefly of varying degrees of vasospasm Coolness of the fingers may be present as well as cyanosis of the extremity particularly of the hand The color change is generally diffuse although in some instances mottling may be observed There is no obvious involvement of the radial or ulnar arteries However the vessels may be difficult to palpate because of the swelling At times the oscillometric readings may be somewhat reduced as compared with the opposite normal side although the blood pressure in the involved limb is usually normal

DIFFERENTIAL DIAGNOSIS

Diagnostic Points The diagnosis of primary thrombosis of the axillary or subclavian vein should present little difficulty The rapid onset of a diffuse swelling of an upper extremity in an otherwise normal individual associated with comparatively little pain and no constitutional reactions are pertinent points in this regard Other signs of value are cyanosis and coolness of the fingers distended cubital veins an increase in venous pressure prominence of veins extending from the arm onto the chest wall and the presence of a tender cordlike mass in the course of the axillary vein

Secondary Thrombosis Primary thrombosis must be differentiated from thrombosis secondary to a number of different conditions Among these are polycythemia cachexia and congestive heart failure [17] In the case of the latter however the thrombotic episode is usually a terminal incident and hence offers no difficulty in differential diagnosis Mediastinal tumors and aneurysms of the ascending aorta may cause compression of the innominate vein and also contribute to venous thrombosis

Thrombosis or obstruction of the axillary vein may be caused by various local factors For example metastasis to the axillary lymph nodes from primary carcinoma of the breast or from other types of neoplasms may either directly invade the main venous channel or exert external pressure on it Concomitant blockage of the lymphatic vessels further contributes to the edema associated with such a clinical picture However there should be no difficulty differentiating this state from primary thrombosis First the swelling shows little tendency to recede and may in fact become more marked Second pain is generally present in the shoulder neck and arm being caused by involvement of the brachial plexus by the malignant neoplasm [31] It is persistent severe and progressive and may be followed by paralysis of the limb Finally collateral venous channels are generally observed for some time before the appearance of edema while in primary thrombosis these vessels become noticeable only after the swelling is beginning to regress (For discussion of *Secondary Lymphedema* see Chap XXII)

Gradual obstruction of the axillary vein may also be produced by scar tissue formation consequent to radical removal of the breast ... permanently ... thrombo... ...is maintained in a dependent

position Another mechanical basis for thrombosis is alteration in the course of the axillary vein following removal of the pectoral muscles [30]

Other Causes for Enlargement of Arm Besides venous stasis swelling of the upper extremity may be due to a number of different conditions The most common is interference with lymphatic outflow, as is present after extensive cellulitis associated with lymphangitis and lymphadenitis or following blockage of lymphatic channels (Chap XXII) An arteriovenous aneurysm may likewise produce enlargement of the upper extremity because of the large amount of blood flowing into the superficial veins from the fistula In both instances there should be no difficulty in differentating them from primary thrombosis of axillary or subclavian vein (For the differential diagnosis of swelling see Chap VI)

Treatment

Therapy in primary thrombosis of the axillary or subclavian vein consists chiefly of attempts to control the swelling Bed rest, elevation of the upper extremity on pillows, and the use of warm moist dressings will generally accomplish this through facilitation of venous and lymphatic outflow and the elimination of venous and arterial spasm Movement of the hand should be encouraged from the outset, since exercise promotes emptying of the lymphatics and veins improves the arterial circulation and discourages propagation of the thrombus Repeated cervicodorsal paravertebral sympathetic blocks may be of value if signs and symptoms of vasospasm are prominent Sympathetic blocking agents may also be used under these circumstances

Although the question as to whether or not anticoagulants should be administered has not been fully settled the fact that occasionally pulmonary embolism has followed primary axillary vein thrombosis gives support to the view that such medication is advisable in the acute phase of the condition However it has not been conclusively shown that this therapy facilitates the formation of a more rapidly functioning and adequate collateral circulation by preventing propagation of the thrombus into venous subdivisions

After the swelling has disappeared or is minimal and the patient is symptom free he should be allowed to become ambulatory and to use his arm but instructed to avoid strain on it Placing the limb in a sling and the use of an elastic bandage may help control residual edema If a certain position assumed during daily work was conceivably the original cause for the thrombosis then this should be eliminated or used infrequently for otherwise there may be a recurrence no matter how trivial the strain might be

If incapacitating edema or pain persists for several months after the acute episode, surgical procedures may have to be tried Excision of the segment of thrombosed vein has been recommended on the possibility that it is acting as a focus of irritation for the initiation of vasospasm Removal of the obstructing thrombus has also been suggested However the advisability of such measures is questionable, since in the first case the possibility of recanalization of the thrombus is lost, while in the second recurrence of the thrombotic process is likely Furthermore, an exploration of the axillary and subclavian veins is a difficult

undertaking and each ligated vessel necessitated by the operation becomes a handicap to the collateral circulation regardless of how small it is[13]

Prognosis

The outlook in primary axillary and subclavian vein thrombosis is excellent as far as life is concerned no deaths having been reported However if the collateral venous circulation is inadequate a postthrombotic syndrome may develop leading to swelling which may persist for years and a sense of heaviness or dull aching whenever the limb is exercised At times pain and discomfort may be permanent Furthermore there is always the possibility of recurrence if the precipitating movements are continued Still in most instances the patient becomes relatively free of symptoms several months after the acute episode and is able to resume light work However it is questionable whether complete recovery ever occurs since a certain amount of swelling and discoloration generally persists The collateral circulation although usually adequate for mild exercise rarely becomes efficient enough to cope with vigorous physical work

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CHAPTER XV VASCULAR DISORDERS AFFECTING THE VENOUS SYSTEM (*Continued*)

3 PULMONARY EMBOLISM

The most serious complication of thrombosis of the veins in the extremities is pulmonary embolism Not only is it responsible for a significant percentage of the mortality associated with surgical procedures but statistical studies of routine postmortem examinations have revealed that in from 0 3 to 2 5 per cent of the cases massive pulmonary embolism is the cause of death If one adds to this number the numerous examples of clinically recognized nonlethal pulmonary emboli it is apparent that the condition is by no means as uncommon as was once generally believed

Sites of Origin

The clinical picture is the result of blocking of the pulmonary artery or its branches by a clot originating at some distant point in the venous system One of the most frequent locations for the origin of an *embolus* is the deep venous plexuses of the lower extremities especially those in the calf muscles and the small muscles of the foot However a *thrombus* in the iliofemoral vein which propagates beyond its point of attachment may also break off and lodge in the lungs Furthermore pulmonary infarction followed by abscess formation is a relatively frequent complication of septic thrombophlebitis of the pelvic veins In the male the prostatic plexus of veins is likewise a source of emboli Even simple thrombosis of superficial veins of the lower limbs may be followed by the liberation of clots which eventually enter the deep venous system This is particularly true in thrombosis of a varicose vein in the elderly patient and traumatic superficial thrombophlebitis On the other hand superficial migratory thrombophlebitis associated with thromboangiitis obliterans thrombophlebitis migrans chemical thrombophlebitis and superficial and deep thrombophlebitis of the upper extremities are rarely followed by pulmonary embolism

Pathogenesis

The seriousness of pulmonary embolism will depend upon the following (1) the size and importance of the vessel or vessels occluded (2) the existence of

underlying pulmonary pathology (3) the presence or absence of infected material in the emboli, and (4) the degree of associated vasospasm of the pulmonary arteries

Sudden massive obstruction of the pulmonary circulation may produce acute dilatation of the right ventricle (*acute cor pulmonale*) and death For this to occur there must be blocking of more than half of the pulmonary bed as might take place if the embolus partially obstructed the pulmonary artery or if a large clot was trapped in each lung (Fig 34) The great reserve possessed by the pulmonary circulation is due to the ready distensibility of the small vessels and to the exist



Fig 34 Pulmonary embolism in vessels of both lungs causing extensive infarction

ence of large numbers of capillaries which although ordinarily not functioning can quickly be called upon when needed However if pulmonary edema coexists the deleterious effects of pulmonary embolism are markedly accentuated In fact some workers in the field believe that in the absence of this factor occlusion *of pulmonary vessels* other than the main artery and its large branches will not be followed by clinical pulmonary infarction

Repeated showers of small emboli generally have much less deleterious effects than a single massive one although if the episodes are frequent enough the combined infarcted areas may eventually produce severe cardiac embarrassment In the case of infected emboli which are usually multiple the prognosis is particularly poor because of the widespread production of small lung abscesses

Other factors which may contribute to the seriousness of the condition are the

degree of reflex vasoconstriction of noninvolved pulmonary arteries and vagal overactivity If vasospasm is marked it may cause death even though the vessels actually occluded by the embolus are not of major importance Recent experimental evidence has again emphasized the possibility that there may be a vagal element along with anoxia to explain such findings in pulmonary embolism as the rapid decline in systemic blood pressure the slow cardiac rate and abnormal changes in the electrocardiogram Associated reflex bronchial constriction and reflex increase in bronchial secretion may be present probably also on the basis of vagal activity

Pathology

Depending upon the various factors mentioned above pulmonary infarction may or may not take place With massive pulmonary embolism this type of change does not occur nor will it be noted if the emboli are minute and occlude only the terminal pulmonary vessels Obstruction of the smaller pulmonary arteries generally results in the formation of infarcts particularly if the site of occlusion is at a region where two or more pleural surfaces meet The lesions may vary in size from 0 5 to 10 cm[8] They are usually multiple most of them being located in the lower lobes especially at the costophrenic angles

The microscopic changes in the lungs vary according to the age of the process In the first two days there is marked congestion of capillaries with diapedesis of red blood cells into the alveoli The latter are filled with debris On the third day necrosis of the alveolar wall occurs with an associated breakdown of red blood cells Organization takes place within the second week In some instances in which there is incomplete infarction the process is usually terminated by resolution within four days

CLINICAL CHARACTERISTICS

The onset of pulmonary embolism is generally sudden If a large branch of the pulmonary artery or the main vessel itself is blocked the clinical picture is frequently heralded by anxious facies labored breathing and air hunger cyanosis severe substernal pain rapidly falling systemic blood pressure and shortly afterward death Pulmonary edema may likewise be present The substernal oppression may possibly be attributed to the acute cor pulmonale which invariably follows a massive obstruction of the pulmonary circulation If the patient survives the initial catastrophe subsequently fever cough localized chest pain of a pleuritic type and expectoration of clotted blood will appear The hemoptysis generally persists for two or three weeks There may also be signs of right heart failure such as epigastric discomfort from liver engorgement and increased venous pressure

If the involved vessel is small the initial manifestations are mild in nature consisting of slight pleuritic pain with or without cough and bloody expectoration In some instances the signs of pulmonary infarction may not be noted for several days after the embolism occurred

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If the involved vessel is small, the initial manifestations are mild in nature, consisting of slight pleuritic pain with or without cough and bloody expectoration. In some instances the signs of pulmonary infarction may not be noted for several days after the embolism occurred.

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Differential Diagnosis

Myocardial Infarction During the early period of massive pulmonary embolism, the condition may be confused with acute myocardial infarction, since in both states severe substernal pain and signs of shock may occur However as already pointed out the electrocardiographic alterations and the evolution of the pattern generally help in making the differential diagnosis as do the physical findings in the lungs and the x ray changes The clinical story is also of value, particularly with regard to the type of onset of the two disorders Pulmonary embolism is ushered in suddenly while in myocardial infarction the symptoms appear more gradually, with significant premonitory changes frequently preceding the critical state by several hours or days Chest pain in pulmonary embolism is sharp pleuritic and has no typical localization in contrast to the symptoms of myocardial infarction which are of a pressing or constricting type being located substernally with radiation to the shoulders and arms Dyspnea and cyanosis are often intense in pulmonary embolism while in myocardial infarction they are generally mild or not present at all Fever leukocytosis and an increased sedimentation rate are observed early in pulmonary embolism and are relatively late phenomena in myocardial infarction

Lobar pneumonia Since pulmonary infarction is frequently associated with such findings as hemoptysis pleural pain fever and physical and x ray findings of consolidation in the lungs it is obvious why lobar pneumonia should always be considered in the differential diagnosis The history of previous episodes of pulmonary embolism or deep thrombophlebitis or the existence of the acute phase of deep thrombophlebitis would favor the diagnosis of pulmonary infarction Significant also is the fact that the onset of hemoptysis frequently occurs shortly after the appearance of the pain in the chest the sputum immediately containing blood clots which persist for a week or two On the other hand in lobar penumonia the sputum is rusty in color and very rarely demonstrates clotted blood The x ray may be of help if the typical wedge shaped type of lesion associated with pulmonary infarction is present

Atypical pneumonia At times showers of emboli may make the differential diagnosis between pulmonary infarction and atypical pneumonia a difficult one Physical examination, x ray findings and the electrocardiogram may be of little use in this regard The appearance of a venous thrombosis before or shortly after the lung changes are noticed helps confirm a diagnosis of pulmonary emboli

Primary Pulmonary Artery Thrombosis The differentiation of this condition from pulmonary embolism is generally not possible clinically the diagnosis for the most part resting on the postmortem examination However, rarely is pulmonary artery thrombosis as ociated with the sudden severe shocklike state which follows a massive pulmonary embolism

Other Conditions Less commonly confused with pulmonary embolism are a number of other conditions Among these are cardiovascular disorders such as acute heart failure paroxysmal tachycardia and dissecting aneurysm Certain respiratory disorders as for example spontaneous pneumothorax and pulmonary atelectasis must also be considered in the differential diagnosis

infected emboli which may manifest themselves as sites of local pneumonitis However, at times even the latter may demonstrate no change until abscess formation has occurred *In the case of relatively large infarcts, the* signs may be similar to those present over a consolidated lung of lobar pneumonia Atypical physical findings may also be noted If the involved portion of the lung extends to the periphery, so that irritation of the pleura is produced a friction rub may be heard

Physical examination of the heart may reveal findings suggestive of pulmonary artery and right ventricular dilatation Forceful pulsations of the pulmonary artery may be evident with increased dullness on percussion in the region of the pulmonary conus Marked accentuation of the pulmonic sound is generally present as a result of an elevated pressure in the pulmonary circulation This may be associated with a *loud* blowing systolic murmur in *the* pulmonic area *Later* a state of chronic cor pulmonale may supervene

Diagnostic Aids

Electrocardiographic Findings Certain changes may be noted in the electrocardiogram probably in part due to the acute dilatation of the right ventricle In the limb leads these tend to resemble the posterior wall type of myocardial infarction There may be a Q wave in Lead III and either a depression of the S T segment in leads I and II or an S wave staircase phenomenon ' The T wave may be inverted in Leads III V_1 V_2 and V_4 Other findings are sinus tachycardia, right bundle branch block auricular arrhythmias, and shifting of the transition zone to the left Rarely are all these changes seen in any one set of records Furthermore in a great number of cases the alterations which do occur are of no diagnostic significance They *are frequently transient in nature and do not conform* to any type of pattern change such as is noted in the course of myocardial infarction The evolution of the variations is also more rapid than in the case of the latter The most that can be said for the electrocardiogram as a diagnostic aid in pulmonary embolism is that in some instances it may supply valuable confirmatory evidence while in others *it* is of little use

X ray Findings The changes in the x ray in pulmonary embolism when clear cut are frequently sufficient to make the diagnosis They are generally apparent within 24 hours after the onset of the condition although in some patients they may not be observed for several days Typically the lesion has a wedge shaped appearance and *is usually located in the left lower lobe In the initial stage the* diaphragm on the affected side tends to be elevated A comparative increase in hilar shadows which subsequently recedes is also considered significant

Unfortunately the characteristic x ray *picture is not always* observed *Frequently* the changes may be misinterpreted as representing a pleurisy or a patch of typical or atypical pneumonia It must also be remembered that since a pulmonary embolus is not necessarily *followed* by infarction of lung parenchyma under some circumstances the x ray will show no abnormalities Therefore as in the case of the electrocardiogram this measure may either be of great or of little or no diagnostic importance

prevention of further episodes far outweighing the value of anticoagulant therapy In fact it is only in recent years that the advantages of combining the two have begun to appeal to them On the other hand there are others who are equally strong in their opposition to the use of vein ligation and who feel that as good or even better results can be expected from anticoagulant therapy alone When contraindications to anticoagulants exist (pp 480 and 484) there is almost general agreement that surgical interruption should be carried out The veins on which this is done are the femoral the common iliac and the inferior vena cava

Ligation of Femoral Vein Distal to Junction of Deep Femoral Vein This is the most commonly performed procedure being used both prophylactically in individuals who are predisposed to pulmonary embolism and for the active treatment of the condition In most instances little interference in venous return results In the limb in which such a procedure has been done the average fall in venous pressure with walking (p 407) is practically the same as that observed in the normal individual[11] This is because channels still exist through which blood can leave the limb The lack of sequelae is probably respon ible in part for the widespread use of the operation

However there are certain possible complications of and weaknesses inherent in the procedure To be considered is the fact that it is by no means as simple and innocuous as it was originally considered[2 3] First there is always the risk of loosening an embolus or of damaging adjacent vascular structures particularly the femoral artery Second a thrombophlebitis distal to the ligature may also result Third thrombi may form on the portion of the vessel immediately proximal to the ligature

Besides the possibility of untoward effects ligation of the femoral vein below the junction of the deep femoral vein does not necessarily prevent pulmonary emboli[4 6 7] It is of interest in this regard that an extensive study on autopsy material has revealed that when thrombi are present in the pelvic veins their location is most often proximal to the usual point of ligation[9] It is also true that clot forming in a patent deep femoral vein can enter the inferior vena cava via the femoral vein and furthermore that in some patients there may be a communication between the femoral and the deep femoral veins at a lower level (p 430) Finally the operation does not have any effect on emboli arising in the pelvic or pro tatic venous plexus

Ligation of the Femoral Vein above the Junction of the Deep Femoral Vein Such a procedure is almost invariably followed by evidence of marked interference with venous return and a clinical picture resembling iliofemoral thrombophlebitis Consequently the operation has found few advocates Still in certain circumstances it is performed in preference to low femoral vein ligation as for example when the thrombotic process has propagated into the lumen of the femoral vein The possibility that this vessel may appear normal in the segments exposed surgically and still contain clotted blood in a more distal inaccessible portion is another point in favor of its ligation

Ligation of the Common Iliac Vein Although this operation has had very little clinical trial it appears to have some advantages in that it will prevent

TREATMENT OF PULMONARY EMBOLISM WITH INFARCTION

The therapeutic approach to pulmonary embolism involves first, prevention of its formation second steps to combat pulmonary embarrassment and finally means to hinder subsequent episodes of infarction Since prophylaxis is similar to that employed in deep venous thrombosis of the lower extremities, the following section will deal only with the other two points (For discussion of *Prophylactic Measures*, see Chap XIV)

Medical Therapy

Treatment of the Local Process in the Lungs Therapy for the acute stage of pulmonary infarction is for the most part symptomatic Shock should be counteracted by the usual methods, although in most instances if the embolus is large enough to produce such a state the condition of the patient is precarious and most therapeutic procedures are of no avail If there is cyanosis due to interference with aeration of the blood an oxygen mask is efficacious, at times even life saving Besides raising the oxygen content of the blood, it reduces the respiratory rate and thus decreases the amount of pleuritic symptoms experienced with inspiration Pain may have to be controlled by the use of narcotics or by the slow intravenous administration of procaine (500 cc of 0 1% solution) It is necessary to point out however, that although the latter procedure also helps reduce dyspnea and allays anxiety and a sensation of imminent death at the same time it adds a large quantity of fluid to the circulating blood volume thus placing a further burden on an already overtaxed cardiovascular system On the basis that there is an associated spasm of unaffected normal pulmonary vessels the slow intravenous injection of papaverine (97 mg 1½ gr) and atropine sulfate (0 65 mg, 1/100 gr) may be a worthwhile early measure Sympathetic blocking agents (Chap XXX) should likewise be tried If there are signs of right heart failure the usual treatment for this condition should be instituted Because of the possibility of pneumonitis developing in the infarcted area the prophylactic administration of antibiotics is indicated No treatment is required for the hemoptysis which generally disappears spontaneously in one to two weeks

Use of Anticoagulants Anticoagulants should be started at once to prevent further episodes of pulmonary infarction as well as to reduce the tendency for the clot to propagate in the pulmonary bed Both heparin and dicumarol should be given at first and then heparin should be discontinued when the prothrombin activity has been lowered to the therapeutic level by dicumarol This state should be maintained by the continued use of dicumarol until the patient has been ambulatory for four or five days (See *Combined Administration of Heparin and Dicumarol*, Chap XXIX)

Surgical Therapy

General considerations Whether or not vein ligation should be performed immediately upon diagnosis of pulmonary embolism is not certain Some workers[1, 2] are quite emphatic in their opinion that this is the most important step in the

6 ERB W H and SCHUMANN F An appraisal of bilateral superficial femoral vein ligation in preventing pulmonary embolism Application of procedure in 100 controlled cases of fracture of femoral neck *Surgery* 9 819 1951
7 GORDON C A ROSENTHAL A H and O LEARY J L Venous thrombosis and pulmonary embolism *Am J Surg* 83 556 105
8 HAMPTON A O and CASTLEMAN B Correlation of postmortem chest teleoroentgenograms with autopsy findings with special reference to pulmonary embolism and infarction *Am J Roentgenol* 43 305 1940
9 McLACHLIN J and PATERSON J C Some basic observations on venous thrombosis and pulmonary embolism *Surg Gynec & Obst* 93 1 1951
10 NORTHWAY R O and BUXTON R W Ligation of the inferior vena cava *Surgery* 18 85 1945
11 O KEEFE A F WARREN R and DONALDSON G A Venous circulation in lower extremities following femoral vein interruption *Surgery* 9 67 1951
12 O NEIL E E Ligation of the inferior vena cava in the prevention and treatment of pulmonary embolism *New England J Med* 232 641 1945

thrombi arising in the prostatic and uterine plexuses, tributaries of the hypogastric vein, from entering the inferior vena cava

Ligation of the Inferior Vena Cava Surgical interruption of the inferior vena cava just above its formation is performed for certain limited objectives[101] The first is a situation in which one or more pulmonary infarcts have occurred whose source is obscure, the rationale for such a step is that the veins of the lower extremities are most often the site of pulmonary emboli Second, the procedure has been utilized when there is no question that the location of the thrombotic process is in the legs or feet, or in the pelvis Third, it would appear to be the operation of choice when both femoral veins are involved and the alternative is an attempt to suck out the entire thrombus separately from the proximal segment of each vessel Frequently the latter procedure is unsuccessful, and there is the additional danger of dislodging some of the clot in the process Finally, inferior vena caval ligation is indicated when thromboembolic disease follows transurethral resection

Because of the rich collateral venous circulation which develops soon after operation (p 433) usually only minimal symptoms result from the procedure such as heaviness moderate swelling, and numbness In fact, the degree of immediate postoperative edema is not as pronounced as that which follows division of both femoral veins above the termination of the deep femoral vein and in time, usually clears up However, it may increase when the patient becomes ambulatory, and hence elastic stockings are required for at least one year following ligation Stasis ulcers have been also reported in some instances

PROGNOSIS

In the presence of a pulmonary embolism, the prognosis will depend upon the degree of embarrassment of the pulmonary circulation If this is considerable death may be sudden If the patient survives the initial shock the outlook is good provided secondary infection of the infarcted portion of lung can be prevented

Once the patient has recovered from the condition, he generally shows little reduction in pulmonary or cardiac reserve However, subsequent attacks of pulmonary embolism may cause enough further embarrassment to be fatal or to result in a permanent reduction in function of the cardiovascular and pulmonary systems (chronic cor pulmonale)

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2 ALLEN A W The present evaluation of the prophylaxis and treatment of venous thrombosis and pulmonary embolism *Surgery* 26 1 1949

3 ALLEN A W and DONALDSON G A Venous thrombosis and pulmonary embolism *Bull New York Acad Med* 24 619 1948

4 ANLYAN W G CAMPBELL F H SHINGLETON W W and GARDNER C E JR Pulmonary embolism following venous ligation *Arch Surg* 64 00 1952

5 CORT J H and DAVIS G D Observations on the role of vagal activity in the effects of pulmonary embolism *Yale J Biol & Med* 22 213 1950





Fig 35 Postphlebitic syndrome A Marked secondary varicosities following right iliofemoral thrombophlebitis B Collateral vessels in suprapubic area after left iliofemoral thrombophlebitis

CHAPTER

XVI VASCULAR DISORDERS AFFECTING THE VENOUS SYSTEM (*Continued*)

4 CLINICAL MANIFESTATIONS OF VENOUS STASIS AND THEIR TREATMENT

Venous stasis implies a chronic pooling of blood in and an overdistension of the superficial veins of the lower extremities If present for more than 4 or 5 years this state may produce dilated and varicose veins edema signs of excessive sympathetic tonus, pigmentation stasis dermatitis recurrent chronic indurated cellulitis and ulceration At the same time, the patient may complain of night cramps pain and ready fatigue Although noted to some extent in primary varicosities such findings are usually much more prominent following acute deep thrombophlebitis For this reason they are collectively termed the postphlebitic syndrome

DILATED AND VARICOSE VEINS

Pathogenesis

Dilated and varicose veins are frequent sequelae of iliofemoral thrombophlebitis Both the great and the small saphenous systems may be involved the varicosities slowly developing over a period of years and being most apparent in the leg (Fig 35) Generally the changes are secondary to an increase in venous pressure in the deep veins transmitted to the superficial vessels via the communicating branches The resulting distension of the latter two systems leads to incompetency of their valves

The elevated pressure in the deep veins is generally due to regurgitation of blood into them, following destruction of the valves in the process of recanalization of the segment of thrombosed vessel Much less frequently the venous system remains occluded with the result that in the role of returning blood to the heart a greater than normal load is placed on the superficial veins This also produces overdistension of the relatively unsupported thin walled vessels

elastic stocking remains snug fitting At first the heavy weight one way stretch is necessary but later the light weight two way stretch may be substituted

Aside from wearing an elastic stocking during all working hours the patient should observe several other rules for control of the swelling For six months following the acute venous obstruction he should make a habit of lying down twice a day one half to one hour with his legs elevated in order to drain out any fluid which has accumulated At night he should continue sleeping with the foot of the bed elevated 6 to 8 inches Also if at all possible he should not stand in



FIG 36 Postphlebitic syndrome Chronic edema of left leg after left iliofemoral thrombophlebitis

one position for a lengthy period of time Walking is much less conducive to edema formation than is standing since the contractions of the muscles help relieve the venous stasis by their pumping action on the veins

SWELLING ASSOCIATED WITH PRIMARY VARICOSITIES

Treatment

The treatment of the relatively minor swelling associated with varicosities consists of the use of an elastic stocking If the swelling is of any magnitude, elevation

Treatment

Therapy of varicose veins due to deep thrombophlebitis is mainly prophylactic. This involves the use of a well-fitting elastic stocking applied immediately after the patient has recovered from the acute stage of the disease and is becoming ambulatory. Such a measure shunts the blood from the superficial veins, where it ordinarily meets little resistance to flow, into those deep venous channels which are still patent. As a result, the development of deep collateral vessels is encouraged. Such an effect is desirable, since these veins carry blood more efficiently during muscular activity, and, in addition, they do not tend to become varicose because they have better support. At the same time the superficial veins are spared and hence venous stasis is in great part prevented.

The problem of how to deal with existing varicosities secondary to deep thrombophlebitis has not been fully solved. Some workers believe that regardless of the cause varicose veins are ineffective in the removal of blood from the limb and therefore they should be treated surgically. Accordingly, they advocate proximal interruption of the great and small saphenous veins, with a stripping of these vessels for the full length of their course, and at the same time, ligation of the femoral vein below the junction with the deep femoral vein.[5] In practice, such a procedure is rarely carried out for secondary varicosities unless they are associated with treatment-resistant ulceration.

There are other workers who feel that in the presence of a block in the deep venous system or an incompetency of the main venous valves, ligation or stripping of superficial varicose veins may produce untoward effects since under such circumstances very few venous channels are left for removal of blood from the limb. The question always arises as to whether all superficial veins which are dilated as a result of a block or incompetency of the deep venous system are likewise incompetent and in need of removal or compensatory and hence useful.[13] It would seem, therefore, that only very carefully selected cases of postphlebitic syndrome should be subjected to peripheral vein surgery.[1]

SWELLING*

Postphlebitic Edema

Treatment

One of the most frequent findings of the postphlebitic syndrome is pitting edema of the involved extremity (Fig. 36).† If this change persists uncontrolled over a long period of time, it will be replaced by a brawny nonpitting lymphedema. In order to prevent such a reaction it is necessary for the patient to continue using an elastic stocking until a trial period of physical activity without it is followed by no return of the swelling. It may take several months to years before this aid can be discarded, depending upon the rapidity of formation of an adequate collateral venous circulation. Care must be taken at all times to see that the

* See Table 9, p. 86.
† For pathogenesis see *Pathologic Edema*, Chap. XXVIII.

to the abdomen or directly to the involved limb will help alleviate the discomfort Sympathetic blocking agents like Priscoline Hydergine and Dibenzyline are also worthy of a clinical trial Usually however there will be a gradual reduction in the severity of the symptoms with the passage of time

PIGMENTATION

Pathogenesis and Clinical Characteristics

Brownish pigmentation is a relatively frequent finding in the presence of venous stasis being generally located in the lower third of the leg (Fig 37A) Infrequently it is noted as the sole sign of venous impairment There appears to be no direct relationship between the degree of pigmentation and the severity of the under lying condition and often long standing varicosities may show no signs of this response

The basis for the pigmentation is not known It has been thought by some workers that it follows the deposition of hemosiderin in the tissues Others believe that it represents capillary hemorrhages due to the high venous and capillary pressure present with venous stasis [5]

Treatment

There is no definitive treatment for the pigmentation Usually if the venous stasis is controlled further deposition is prevented At times there may even be some regression in the intensity of the color under these circumstances but in most instances the condition remains stationary Besides their ugliness the areas of pigmentation have significance since they represent locations of reduced re sistance to trauma and infection and hence potential sites of ulceration

STASIS DERMATITIS

Clinical Characteristics

Stasis dermatitis is generally noted after the edema due to varicosities or deep thrombophlebitis ha existed for some time and [illegible] ers have occurred It [illegible] it may take the form [illegible] intense itching and [illegible] persistent scratching the condition is exaggerated Super ficial oozing of serum may be present or the lesion may be covered by scaly corni fied skin surrounded by an area of redness or brown discoloration (Fig 37B)

Treatment

Therapy in stasis eczema consists first of the control of venous stasis (p 282) and then the use of local therapy Of the latter coal tar products (Daxalan oint ment—see below) and the continuous application of Burrow's solution 1 20 or of a dilute solution of silver nitrate (15 cc of a 10% solution in 1 liter of distilled

of the foot of the bed is advisable The patient should also attempt to limit the amount of time he spends standing in one position

EXCESSIVE SYMPATHETIC TONUS

Pathogenesis and Clinical Characteristics

The postphlebitic extremity may demonstrate signs of excessive sympathetic tonus, such as cyanosis lowered skin temperature and increased sweating of the



FIG 57 Results of prolonged venous stasis A Brown pigmentation in long standing varicosities B Hyperkeratosis associated with varicosities C Chronic indurated cellulitis with superimposed ulceration

feet The response is evidently related to stimulation of the sympathetic nerves perhaps through a reflex initiated by the segment of thrombosed vein acting as a focus of irritability It is also possible that the long period of physical inactivity to which patients with deep thrombophlebitis may be subjected is in part responsible

Treatment

Generally, no specific therapy is necessary to combat the vasospasm since the symptoms are annoying rather than disabling At times the application of dry heat

to the abdomen or directly to the involved limb will help alleviate the discomfort Sympathetic blocking agents like Priscoline, Hydergine and Dibenzyline are also worthy of a clinical trial Usually, however there will be a gradual reduction in the severity of the symptoms with the passage of time

PIGMENTATION

Pathogenesis and Clinical Characteristics

Brownish pigmentation is a relatively frequent finding in the presence of venous stasis being generally located in the lower third of the leg (Fig 37A) Infrequently it is noted as the sole sign of venous impairment There appears to be no direct relationship between the degree of pigmentation and the severity of the underlying condition and often longstanding varicosities may show no signs of this response

The basis for the pigmentation is not known It has been thought by some workers that it follows the deposition of hemosiderin in the tissues Others believe that it represents capillary hemorrhages due to the high venous and capillary pressure present with venous stasis[5]

Treatment

There is no definitive treatment for the pigmentation Usually if the venous stasis is controlled further deposition is prevented At times there may even be some regression in the intensity of the color under these circumstances but in most instances the condition remains stationary Besides their ugliness the areas of pigmentation have significance since they represent locations of reduced resistance to trauma and infection and hence potential sites of ulceration

STASIS DERMATITIS

Clinical Characteristics

Stasis dermatitis is generally noted after the edema due to varicosities or deep thrombophlebitis has existed for some time and before ulcers have occurred It is usually of the weeping eczematous type although at times it may take the form of an erysipeloid infection There is frequently an associated intense itching and as a consequence of the persistent scratching the condition is exaggerated Superficial oozing of serum may be present or the lesion may be covered by scaly cornified skin surrounded by an area of redness or brown discoloration (Fig 37B)

Treatment

Therapy in stasis eczema consists first of the control of venous stasis (p 282) and then the use of local therapy Of the latter coal tar products (Daxalan ointment—see below) and the continuous application of Burrow s solution 1 20 or of a dilute solution of silver nitrate (15 cc of a 10% solution in 1 liter of distilled

water) may be of benefit in decreasing the severity of the condition A combination of copper sulfate and zinc sulfate (Dalisol) is also useful One packet is dissolved in one quart of water and compresses are applied for hourly periods, with two hours intervening It is essential to eradicate fungus infections of the feet since they may contribute not only to the dermatitis but also to ulceration of the skin (For measures to accomplish this, see *Local Care of the Extremities*, Chap XII)

CHRONIC INDURATED CELLULITIS

Pathogenesis and Clinical Characteristics

The underlying mechanism responsible for chronic indurated cellulitis is chronic edema followed by a low grade inflammatory reaction and local thrombosis of the superficial veins The characteristic lesion consists of a hard localized area of induration affecting the lower third of the leg usually on the medial, although occasionally on the posterior, surface There is a tendency for the process to recede into brawny induration and then to flare up into an acute stage with a hard scalloped inflamed border An area of fibrosis may eventually encircle the entire leg so that a tight constricting band is formed (Fig 37C) The condition is associated with pain locally and at times systemic responses Movement of the limb may *cause aggravation of the symptoms Ulcer formation in the involved site is a fairly* common complication

Treatment

Medical therapy in chronic indurated cellulitis is for the most part unsatisfactory *A period of bed rest with elevation of the limb should be tried and the area* should be exposed to hot soaks for several days Antibiotics should be given parenterally Roentgen therapy has also been used with some reported good results [11] *The optimal dose is 80–100 r (in air) at 200 Kv and 20 ma The focal* skin distance is 50 cm with a medium Thoraeus filter An area of 400 square centimeters or less is exposed each time, with an interval of 2 7 days between consecutive applications Most patients require 1 3 treatments to *the involved* areas

If conservative therapy does not bring obvious improvement, then surgical intervention may be necessary All abnormal structures of the involved area including subcutaneous tissue fascia and devitalized skin are removed and a split thickness skin graft is applied over well vascularized muscle so as to cover the defect At the same time incompetent communicating veins encountered during the operation are ligated If varicosities exist the great saphenous vein is ligated at the saphenofemoral junction and stripped to just below knee level [6] When deep veins are also incompetent ligation of the femoral vein is performed below the junction with the deep femoral vein

STASIS ULCER*

One of the most serious and common sequelae of both deep thrombophlebitis and varicosities is ulceration of the skin (Fig 38) It has definite economic implications since once it has developed it frequently renders the patient a semi invalid incapable of working for weeks and even months Of great importance in this regard is the fact that the condition is notorious for recurrences Very rarely epidermoid carcinoma may develop in a long-standing and neglected varicose ulcer[9 12]

Pathogenesis and Clinical Characteristics

The cause of the stasis ulcer in the lower extremity is the piling up of blood in the superficial veins which eventually builds up a back pressure in the capillaries This acts as an increased filtration pressure to produce a greater movement of fluid out of the vessels into the intercellular spaces Combined with the resulting waterlogging of tissues such factors as anoxia impaired nutrition and accumulation of toxic waste products of metabolism reduce the resistance of the skin Consequently ulceration may follow minor bruises, abrasions or infections or it may even occur spontaneously The medial and less often the lateral aspects of the ankle are the sites of predilection for the stasis ulcer primarily because the protective padding in these locations is poor and the possibility of exposure to trauma is great Furthermore tissues in this portion of the limb seem to have less viability than elsewhere The presence of several communicating veins around the medial malleolus which are poorly supported by surrounding tissues may also contribute to the vulnerability of this region to ulcer formation (For further discussion on this point see *Perforating or Communicating Veins* Chap XXVI for description of the ulcers see *Ulceration of Venous Origin* Chap VII)

Treatment

PROPHYLACTIC MEASURES

The primary treatment of the stasis ulcer is its prevention This involves the steps to combat venous stasis already enumerated in this chapter with regard to the control of edema If primary varicosities are the etiologic agent surgical intervention is also of great value Because the proper management of the acute stage of deep thrombophlebitis helps reduce the subsequent degree of venous stasis this factor is also of importance in decreasing the incidence of ulcer formation

The limb should be protected from even the slightest injury Scrupulous care of the unhealthy skin in the region of the ankle likewise helps prevent ulceration If despite such care a bruise laceration or infection occurs in the involved leg the patient should go to bed for several days with the limb elevated and the lesion should be handled very carefully as regards asepsis Only mild antiseptics should be used Dermatophytosis should be adequately controlled and itching

* See Table 10 p 98

should be treated immediately, since scratching which inevitably follows, may initiate ulceration All these steps likewise apply to the prevention of recurrences of ulcerations

ACTIVE TREATMENT

There is no standardized treatment for the stasis ulcer, although in general the various procedures that have been proposed can be placed into one of the follow



Fig 38 Ulceration resulting from prolonged venous stasis A Extensive ulceration following iliofemoral thrombophlebitis B Ulceration associated with varicosities

ing four categories (1) steps to eliminate venous stasis or to reduce it to a minimum, (2) control of secondary infection (3) local use of substances which stimulate the growth of tissue and epithelialization of the lesion and (4) means to increase local cutaneous blood flow In some instances the ulcer is associated with excruciating pain which requires special measures in its control

Steps to Control Venous Stasis

Bed Rest and Elevation of Limb The ideal approach to the control of venous stasis early in the treatment of the ulcer is complete bed rest with elevation of the

involved extremity Although advantageous there is no real need to hospitalize a patient in order to carry out such a regimen Any adult member of the family can be taught the few fundamental rules that are necessary for home nursing care It is advisable to deny the patient bathroom privileges but if this is not practicable it is essential that he apply a tight Ace bandage to the limb before he gets out of bed Trips to the bathroom should be reduced to an absolute minimum

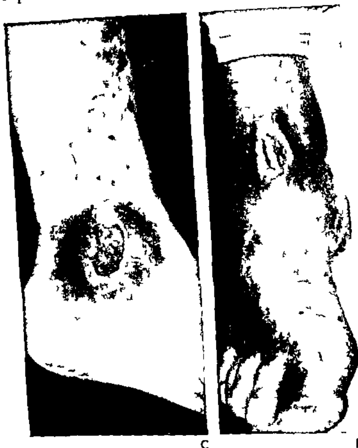


FIG 38 (*Continued*) C Small ulceration due to varicosities demonstrating surrounding area of inflammation in site of predilection for such a lesion D Ulcer associated with varicosities initiated by trauma

Elevation of the limb is best accomplished by raising the two distal supports of the bed 15–25 cm (6–10 inches) with blocks of wood bricks or books The use of pillows for this purpose is not satisfactory since generally the limb either slides off them during the night or sinks down into them Hard pillows placed under the mattress although not as effective as elevation of the foot of the bed may be used when the patient has to share his bed A wedge mattress is also of value[8]

Compression Appliances If the patient is unable to go to bed for the treatment of a stasis ulcer because of financial obligations or other equally important reasons

should be treated immediately, since scratching which inevitably follows may initiate ulceration All these steps likewise apply to the prevention of recurrences of ulcerations

ACTIVE TREATMENT

There is no standardized treatment for the stasis ulcer although in general the various procedures that have been proposed can be placed into one of the follow



Fig 58 Ulceration resulting from prolonged venous stasis A Extensive ulceration following iliofemoral thrombophlebitis B Ulceration associated with varicosities

ing four categories (1) steps to eliminate venous stasis or to reduce it to a minimum, (2) control of secondary infection (3) local use of substances which stimulate the growth of tissue and epithelialization of the lesion and (4) means to increase local cutaneous blood flow In some instances the ulcer is associated with excruciating pain which requires special measures in its control

Steps to Control Venous Stasis

Bed Rest and Elevation of Limb The ideal approach to the control of venous stasis early in the treatment of the ulcer is complete bed rest with elevation of the

The technic of application of a boot is as follows First the lesion is cleaned and covered with sterile gauze and all bony prominences are well padded with cotton to prevent undue pressure Then the impregnated bandage is applied beginning with a circular turn around the foot which is carried up to the ankle and the heel several figure-of-eight turns are necessary to cover the latter[4] No reverse turns are made since on hardening these may press against the skin as a ridge and cause discomfort The next step is to cover the leg This is accomplished by re [illegible] an oblique [illegible] s completed [illegible] below the knee it is allowed to flatten in the air and then is covered by a roller bandage to protect the patient s clothing

The boot is left on for a week or two provided the patient does not experience any symptoms from its use At times considerable secretion from the ulcer may cause sufficient softening of the cast so that venous stasis is no longer controlled If this occurs symptoms are generally aggravated and the boot should be removed Some patients may develop a dermatitis probably due to the accumulation of perspiration within the cast in close contact with poorly nourished skin The materials in the boot may also contribute to the condition The dermatitis generally manifests itself as intense itching which invariably is an indication for immediate removal of the cast

Superficial Vein Ligation or Stripping In all cases of varicose ulcers control of the venous stasis must eventually be effected through surgical obliteration of the involved veins Having determined the sites of incompetency by the various tests used for this purpose (Chap V) the appropriate operation is carried out Special care should be taken to eliminate all varicose veins feeding the ulcer site

The time for surgical intervention is debatable Ideally it should be delayed until the ulcer is clean and infection has been controlled In fact the most propitious period is after the lesion has been healed by medical therapy since under these circumstances the risk of making incisions in infected tissues is eliminated Furthermore the possibility of dealing with venous channels that contain contaminated blood as a result of its passage through the involved area is also excluded However if the ulcer becomes chronic and resistant to medical therapy surgical intervention may become necessary despite its potential dangers

Ligation of Deep Venous System Recently it has been suggested that ligation of the femoral vein below the junction with the deep femoral vein or even of the inferior vena cava is of advantage in treating ulcers in long-standing postphlebitic syndrome It is the opinion of some workers that at the time the femoral vein is ligated ligation and stripping of the great and small saphenous veins should also be performed care being taken to remove the part of the vein underlying the ulcer However ligation of the great saphenous vein is carried out only if temporary occlusion of this vessel and the femoral vein does not produce a significant rise in venous pressure (30 cm water = 2 mm Hg)

Control of Secondary Infection

Elimination of infection is essential for healing of an ulcer This can be accomplished most effectively if the patient is at bed rest Obviously the application of

then it is necessary to resort to another approach for collapsing the veins and controlling venous stasis This involves the application of some type of tight compression to the limb, in the form of an Ace bandage a pure gum rubber bandage an elastic stocking a compression legging or a nonelastic support, like an Unna boot Since some of these measures have already been discussed in Chapter XIV and elsewhere, reference will only be made here to modifications in their use necessitated by the presence of an ulcer

In the treatment of an ulcer, the Ace bandage* is used in conjunction with a piece of sterile sponge rubber, cut slightly larger than the general outline and depth of the lesion The rubber is fitted into the ulcer and then the Ace bandage is applied snugly to the foot and leg up to the knee

In some instances the above measure will cause healing of the lesion, although in general it is not very effective The bandage soon loses its elasticity and then does not exert sufficient tension to prevent venous stasis However, the direct pressure of the rubber on the base of the ulcer does have some therapeutic effect The bandage should be removed every day, the lesion cleaned of secretion and the washed and resterilized piece of rubber reapplied

In order to overcome some of the objections of the compression bandage, a compression legging (see Appendix) has been devised with which a uniform pressure can be applied throughout the lower portion of the leg and foot[10] It consists of an outer duck casing closed with a zipper and an inner butterfly shaped rubber bladder which is inflated through a tube and valve at the top of the legging The hand pump used for inflation has a regulator which automatically controls the air pressure in the bladder An initial pressure of about 35 mm Hg appears to be optimal in most cases However, when the ulcer is located below the malleoli this may not be sufficient to control the venous stasis locally Rather than raising the pressure in the entire balloon it is advisable under these circumstances to place a second smaller bladder below the malleoli and maintain it at a pressure of 50 mm Hg If the entire leg is subjected to this level of pressure discomfort may be produced In the presence of an associated dermatitis a cotton stocking should be worn under the legging to absorb the moisture that ordinarily accumulates on the skin If of a severe degree, the dermatitis should be brought under control by bed rest and appropriate ointments before the legging is applied

According to some workers,[10] the legging is as effective in the healing of varicose ulcers as are bed rest and elevation of the limb The great advantage of the measure is that the patient is able to work while being treated However once the lesion has healed surgical procedures should be instituted to correct and eliminate the venous stasis for otherwise the ulcer may recur when the use of the legging is discontinued

Various types of nonelastic, semirigid boots have also been found of value in the ambulatory treatment of ulcers The most common of these is the Unna gelatin paste boot which however has the technical disadvantage that the chemical mixture with which the gauze bandage is saturated must be melted before it can be utilized Commercially prepared bandages such as the Dome boot (see Appendix), are much more readily and conveniently handled

* A compression bandage consisting of a cotton roll over which a wide elastic bandage is applied appears to have certain advantages over the Ace bandage alone

ointment should be applied with a sterile tongue depressor to the entire ulcer site After the first application it should be left in contact with the lesion for 48 hours and then removed A sharp sterile instrument may be necessary to dislodge all of the ointment which has a tendency to stick to normal skin A certain amount of secretion may be noticed in the ulcer base which is not a contra indication to its further use The coal tar ointment should be reapplied every other day for about 10 to 14 days If no obvious improvement has occurred in that period, it should be discontinued This should also be done if rapid epithelialization is taking place since further treatment may tend to inhibit the restorative process While the material is being applied it is necessary to avoid exposure of the site to direct sunlight or ultraviolet light for tar is a photosensitizer Another untoward effect may be the formation of folliculitis in hairy areas after prolonged use of the ointment

Red blood cell powder (Lyocyte powder) is useful in the treatment of the chronic ulcer It evidently serves as a protective covering and possibly as a source of [illegible]

[illegible] connective tissue The procedure is only of value if the ulcer has been cleaned of secondary infection by the steps outlined above and is not deep Furthermore the continuous formation of a considerable amount of secretion negates its efficacy The technic of application of the red blood cell powder is as follows

The material is liberally sprinkled on the ulcer so as to produce a fairly thick layer over the entire lesion Then the wound is covered with dry sterile gauze and wrapped tightly with gauze bandage The dressing is changed every day or every other day Each time all material not firmly adherent to the wound is washed off with hydrogen peroxide and then more red blood cell powder is sprinkled on the lesion

At times a burning pain is experienced with application of the powder Since this is probably due to the hygroscopic nature of the material it is advisable under these circumstances to substitute a paste of the red blood cell powder made with sterile water and apply it to the ulcer in the form of a compress

Generally with the first application an eschar forms over part of the ulcer the size depending upon the amount of secretion arising from the base If fluid collects below part of the eschar this portion is carefully freed to allow the material to escape No attempt should be made to remove an eschar which is firmly attached However at intervals during the treatment the portion at the periphery of the ulcer should be tested for adherency and if it appears to be free it is peeled off Usually when the latter step can be carried out without pain it indicates that the underlying portion of the ulcer has become epithelialized The treatment is continued until the entire lesion has become entirely covered with normal skin In order for this to occur the patient must continue at bed rest with the involved limb elevated

If despite [illegible] no sign[illegible] indolent and shows to utiliz[illegible] then it is necessary [illegible] One of these is radical excision of the lesion and the surrounding indurated skin and subcutaneous tissues down to the deep fascia

some type of compression bandage, like an Unna boot, prevents such an approach If the ulcer is covered by necrotic tissue all this material should be removed first If it is firmly adherent and can not be separated without causing much pain, then attempts should be made to dissolve the connecting strands For this purpose Varidase and Tryptar (p 501) should be given a trial as well as Azochloramid in oil and Dakin's solution

One of the first measures to use in cleaning up an infected ulcer is wet heat Naturally, this can only be done if the arterial circulation is adequate The simplest procedure consists of covering the ulcer with sterile gauze and wrapping the leg and foot in a turkish towel previously dipped in hot water and wrung almost dry The towel in turn is covered with wax paper oiled silk or some other impervious material External heat is maintained by the use of a heat cradle or a heat lamp An electric heating pad would appear to have some advantage, but there is always the risk associated with placing it around a wet towel should the insulation become faulty The patient should be allowed to regulate the intensity of the heat, using the maximum amount that can be tolerated with comfort The towel must not be allowed to get cold, since this will produce vasoconstriction and interfere with healing The heat should be applied for periods of 3 hours alternating with 1 hour intervals during which the dressings are removed, the leg is dried and the ulcer is covered with a fresh piece of gauze In this manner maceration of skin by the water is prevented

If the ulcer base is infected but not covered by a thick eschar the first step is to take a smear of the secretion so that the bacteria can be cultured and their sensitivity to various antibiotics determined The appropriate medication is then applied locally and on occasion also given parenterally Topical application has been utilized with the following antibiotics in ointment form bacitracin, tyrothricin Aureomycin neomycin and Chloromycetin Tyrothricin has also been used in the aqueous form the compresses being kept moist with a 0 25% solution of the drug

Steps to Accelerate Tissue Growth and Epithelialization

Once infection is controlled and the base of the ulcer is covered by clean granulation tissue the next step is to use substances locally which will stimulate the rate of growth of tissue and epithelialization A large number of substances have been suggested for this purpose Among these are chlorophyll ointment (Chloresium ointment) White s A and D ointment the various dyes like scarlet red and gentian violet, coal tar products (Daxalan ointment) and red blood cell paste or powder From personal experience most of these except the last two have been found to be of little benefit

The coal tar ointments appear to be of value in causing more rapid epithelialization Since some individuals react poorly to them it is advisable to do a routine patch test before beginning the treatment A further precaution is to leave the first application on for 24 hours or less and then carefully observe the skin If there are signs of irritation or if the ulcer appears worse the ointment should be discontinued The production of pain is also a contraindication to its use The

or conversion of the waste products in the muscles or at the myoneural junction

If quinine is ineffective or can not be used because of sensitivity to the drug or a coexisting contraindication there are several other measures which can be tried Among these are diphenhydramine (Benadryl) 50 mg given before retiring[8] large doses of calcium gluconate and dilute hydrochloric acid An electric blanket at night may also reduce the number of attacks

PAIN READY FATIGUE, AND SENSE OF HEAVINESS

Pathogenesis and Clinical Characteristics

Several other symptoms may be experienced by the patient with venous stasis the more common of which are pain ready fatigue and a sense of heaviness The cause for these complaints is not known It is possible that the pressure of the edema on the peripheral nerves and the actual increase in weight of the limb as a result of accumulation of fluid are etiologic factors although at times pain is experienced even when swelling is not present Venous distension by blood at an elevated pressure may also play a role

The pain may be described as an ache a burning sensation a deep pain, a shooting pain or a feeling of compression It is almost invariably present in the calf and the lower portion of the leg and appears to be initiated by standing or placing the limb in dependency It varies in severity and in some instances may be incapacitating Ready fatigue and a sense of heaviness may be experienced in conjunction with the pain

Treatment

There is no effective treatment for the control of t[illegible] However in the case of the postphlebitic u[illegible] severe with the passage of time and in mos[illegible] ttempt should be made to limit the time spent in the upright position If venography and the Valsalva maneuver (Chap XXV) *point to* the existence of an incompetent deep vein ligation of this vessel may relieve the pain and aching in the lower portion of the leg on prolonged standing

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followed by a split thickness skin graft or a pinch graft Such a procedure should be preceded by attempts to eliminate any infection Since excision only removes diseased tissues, it is still necessary to correct the underlying venous stasis

Means to Increase Cutaneous Circulation

In addition to measures to accelerate venous outflow in the treatment of varicose ulcers attempts should also be made to increase cutaneous arterial blood flow, in order to improve the nutrition of the tissues Of value here are sympathetic blocking agents ion transfer with Mecholyl or histamine and, on occasion, even sympathectomy[2] The sympathetic blocking agents worthy of a clinical trial are oral Priscoline 25 mg three times a day, and Hydergine 1 sublingual tablet (0 5 mg) two or three times a day If practicable, 1 ampule of Hydergine (0 3 mg), given intramuscularly once a day, may be substituted for the tablets

Control of Pain

Although in most instances pain associated with a stasis ulcer is readily controlled with local treatment in some cases it becomes very severe the condition resembling a causalgic syndrome As a result, little local therapy is possible because of the aggravation of the symptoms by even the pressure of the bandage The burning and throbbing sensation is usually worse at night and is increased by dependency A lesion producing such a state is generally situated on the medial aspect of the lower third of the leg proximal to the medial malleolus A constant finding is a spot of exquisite tenderness to deep pressure directly over the point where the saphenous nerve pierces the deep fascia of the leg Because of the latter response and because of the neuritic type of pain resection of the saphenous nerve has been suggested for the control of the symptoms[1] (For differentiation of stasis ulcer see *Symptoms simulating pain of ulcers of arterial origin,* Chap I)

NIGHT CRAMPS

Treatment

One of the more common complaints of the patient with moderate varicosities or with a postphlebitic syndrome is night cramps * The treatment of the condition is for the most part palliative In order to reduce the number of attacks it is necessary to decrease the amount of physical effort during the day and to institute the measures to combat venous stasis discussed above It is also advisable to give the patient a clinical trial of quinine sulfate consisting of the oral administration of 0 325 Gm (5 gr) before the last meal at night and a similar dose shortly before retiring[7] In many instances this medication will cause the complete disappearance of symptoms while in others it will reduce the number of attacks However the relief is generally short lived and does not persist after the treatment is terminated The exact mechanism responsible for the therapeutic effect is not known although it is possible that the quinine hastens the removal destruction

* For initiating factors and possible mechanisms responsible for night cramps see p 1[illegible]

CHAPTER

XVII VASCULAR ENTITIES PRODUCED BY TRAUMA OR NOXIOUS AGENTS

I CONDITIONS RESULTING FROM INJURY TO MAIN VESSELS

There are a number of vascular disorders which result from direct injury to arteries or veins in the extremities. Among etiologic agents are wounds produced by machine gun and rifle bullets, high explosive shell fragments, grenades, antipersonnel mine, icepicks, knives, and crushing blows, and even such a relatively minor injury as a wrenched knee. It is also necessary to keep in mind that application of skeletal fixation pins or other surgical procedures may cause accidental trauma to vascular structures. In the evaluation of the degree of damage sustained, the size of the external wound may be misleading, for a small one may still be associated with extensive destruction of the underlying artery and vein, particularly if produced by a high velocity missile. Therefore it is good policy to examine every wound and scar, no matter how trivial, for the possibility of vascular involvement. This is especially true in the presence of injury to nerves, since frequently under these circumstances the neighboring vessels are simultaneously affected.

TRAUMATIC ARTERIAL ANEURYSM

A traumatic arterial aneurysm is a pulsating mass arising from or located in a segment of an artery which follows weakening, stretching, or actual perforation of the wall as a result of injury to the coats of the vessel (Fig 39A). There are two types, the true and the false sacs. In the former the continuity of the vessel wall is still intact but dilatation has occurred due to thinning and distension of the muscle layer. The change may take the form of a uniform fusiform dilatation of a portion of the vessel or of a local saccular outgrowth (Fig 39C). In the false aneurysm complete rupture of the artery has taken place, followed by bleeding into the surrounding tissues. Eventually the clotted material is covered by a wall, the interior of the sac thus formed communicating with the vessel through the original site of rupture. The traumatic aneurysm is generally of this type, although

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notice the appearance of a pulsating mass following an injury A history of intermittent claudication is not elicited since the circulation to the muscles remains adequate If the lesion is large and is located in a confined site symptoms may result from pressure on neighboring nerves

Signs Characteristically an arterial aneurysm manifests the findings of an expansile mass over which a thrill can be felt and a systolic bruit heard (Fig 39A) However if the sac is almost completely filled with laminated clot, these signs may be difficult to elicit or may be absent

Generally very few findings of impaired arterial circulation are noted below the level of the aneurysm Once the sac has formed and is filled with blood the circulation through the arterial channel becomes re-established at practically the previous level of efficiency, unless the clot from the aneurysm extends into the lumen of the vessel, reducing its size

Treatment

Therapy for traumatic arterial aneurysm is surgical If the lesion is let alone there is always the possibility of either further extension rupture into the skin, producing a large hematoma or even rupture through the skin with external bleeding Furthermore the clot which forms in the sac is potentially a source of emboli which may become free in the blood stream and cause complete occlusion of arteries distally located with attendant serious consequences Despite such possibilities, the treatment is rarely a matter of emergency and then only when the aneurysm is rapidly progressing in size or has ruptured

Aneurysmectomy In the presence of an aneurysm of a nonessential artery, the procedure of choice should be complete removal of the lesion However in no case regardless of the type of vessel involved should operation be performed before evaluating very carefully the extent and efficiency of the collateral system using the modified reactive hyperemia test (Chap II) If the response is not satisfactory then aneurysmectomy should be delayed Ordinarily an arterial aneurysm is not a potent stimulus for the formation of a secondary circulation since the distal tissues have adequate blood supply and hence do not suffer from a chronic state of anoxia Therefore preoperatively it is necessary to utilize some means of temporarily reducing the local circulation such as a Matas compressor or a similar type of instrument in order to facilitate the growth of collateral vessels The apparatus is first applied for 5 minutes and then the period is gradually increased until several hours of occlusion of the involved artery are attained without producing any untoward effects

Endoaneurysmorrhaphy (Matas operation) This procedure[4] is of value when the aneurysm is so large that its dissection would most likely result in damage to surrounding muscles nerves and other blood vessels It consists of suturing of the openings of all channels feeding the sac and leaving the latter attached and undisturbed in the wound As in aneurysmectomy the operation should be performed only after an adequate collateral circulation has been demonstrated If the aneurysm is small or accompanied by involvement of nerves endoaneurysmorrhaphy is not indicated because of the possibility of producing damage of

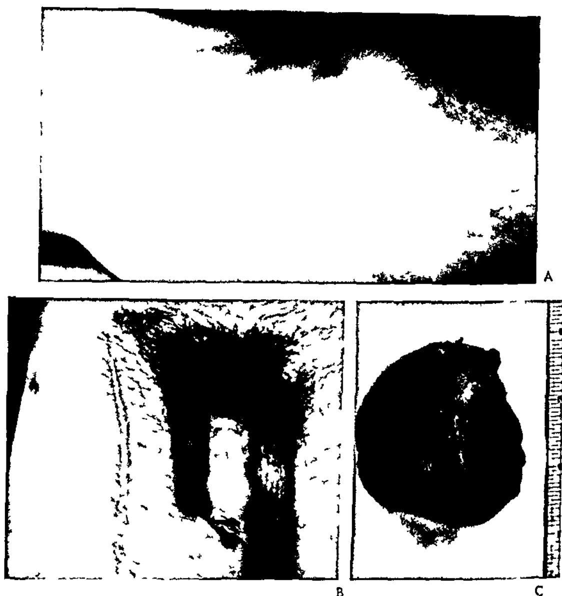


Fig 39 A Femoral arterial aneurysm produced by a bullet B Following surgical extirpation of lesion C Saccular aneurysm removed with probe in femoral artery

a true aneurysm may also form if the injury has caused destruction of only the outer layer of the artery

Traumatic arterial aneurysm of the extremities can occur in almost any location Involvement of the brachial and femoral arteries is somewhat more frequent but all the main vessels are so situated that they are vulnerable to this type of affliction Even traumatic aneurysms of the vessels in the palm have been described, following repeated minor injuries[6]

Clinical Characteristics

Symptoms Complaints associated with an arterial aneurysm are generally vague There may be some pain in the site of involvement and the patient may

notice the appearance of a pulsating mass following an injury A history of intermittent claudication is not elicited since the circulation to the muscles remains adequate If the lesion is large and is located in a confined site symptoms may result from pressure on neighboring nerves

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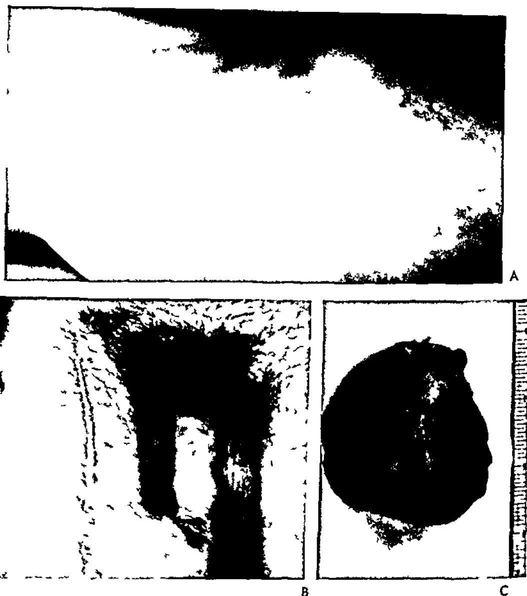


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Clinical Characteristics

Symptoms Complaints associated with an arterial aneurysm are generally vague There may be some pain in the site of involvement and the patient may

being joined to the corresponding vein at approximately the same level Finally, both vessels may open into an aneurysmal sac through a common orifice

Pathogenesis

Systemic Changes In contrast with an arterial aneurysm an arteriovenous fistula is associated with systemic effects of considerable magnitude and frequently of a serious nature With the introduction into the vascular system of a secondary ineffective circuit there is a shunting of a certain proportion of the blood back to the heart via the fistula without passage through the capillary bed In order to compensate for such a situation perpetuated by the maintenance of an area of

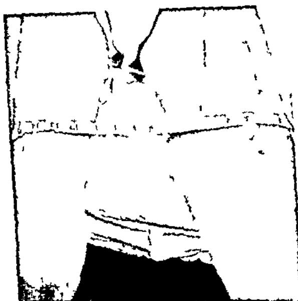


Fig 40 (*Continued*) B After surgical removal of lesion artery and vein ligated distally and proximally and sac extirpated

lowered peripheral resistance the circulating blood volume increases As a result of this response as well as of the greater venous return the rate and force of contraction of the heart are increased thus counteracting the initial fall in systolic blood pressure and raising it to a normal or slightly higher level However the diastolic pressure remains low as a reflection of the reduced peripheral resistance offered by the abnormal communication Eventually the load on the heart causes it to dilate and finally weaken resulting in congestive heart failure

Local Changes In the involved limb there is a marked increase in blood flow into the affected artery most of the circulation being diverted into the veins proximal to the level of the fistula As a result the local venous pressure rises to a level only somewhat less than that in the supplying artery since very little of the energy imparted to the blood by cardiac systole is dissipated in the passage through the fistulous tract In the distal portion of the limb arterial blood flow is markedly

neural structures by the passage of the sutures Under these circumstances, aneurysmectomy is the procedure of choice

Graft Another valuable surgical approach is excision of the entire sac and re-establishment of the continuity of the lumen using a venous transplant or a segment of metal or plastic tubing This procedure is desirable if the aneurysm involves an essential artery and an adequate collateral circulation has not developed Anticoagulants should be utilized for some time before and after surgery, to prevent thrombosis at the operative site

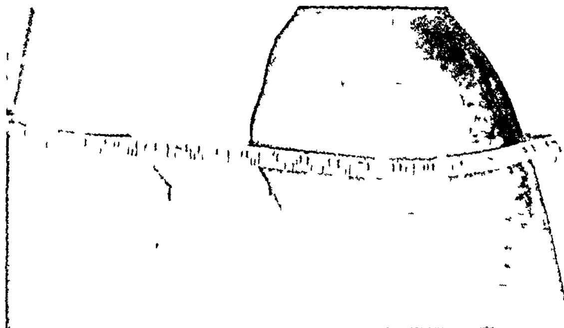


Fig 40 A Femoral arteriovenous aneurysm

Prognosis

The outlook for both the untreated and the treated arterial aneurysm is poor, especially when the popliteal artery is involved The prognosis is best when a successful venous graft has been accomplished With the other procedures, even if nutritional disturbances do not occur postoperatively often the patients subsequently develop intermittent claudication

ACQUIRED ARTERIOVENOUS FISTULA (ACQUIRED ARTERIOVENOUS ANEURYSM)

An acquired arteriovenous fistula is a condition in which there is an abnormal communication between a large artery and companion vein closely incorporated in a common sheath as a result of trauma to these structures Several different types may be produced In one there is a simple direct connection between the two vessels while in another this segment may take the form of an aneurysmal dilatation There may also be an aneurysmal sac arising from the artery with the latter

effective if the arteriovenous fistula is of considerable size so that now *the reduction in heart rate is accompanied by a rise in both systolic and diastolic blood pressure*

Local Signs Fairly typical findings are generally present In all instances a *pulsatile mass* can be palpated in the site of the original injury (Fig 40) This may be so small as almost to escape notice or as large as a grapefruit or greater In most instances a thrill is present over the lesion as well as a continuous murmur with accentuation during systole The latter change is due to the fact that blood is passing from the artery through the communication into dilated venous channels both in diastole and in systole the systolic intensification of the sound resulting from the higher pressure present in the fistula during contraction of the heart If the sac is large the skin over it may be taut thinned out, and red Compression of the main arterial channel above the level of the lesion causes its collapse

There are other signs which reflect the changes in local hemodynamics Because of the marked reduction in cutaneous circulation in the distal portion of the limb *in contrast* to the considerable blood flow through the superficial veins above the level of the fistula the skin temperature in the former site is generally low, while that of the proximal portion is higher than normal The veins in the vicinity of the fistula are large and tortuous resembling varicosities the circumference of this segment of the limb appearing larger than the corresponding portion of the opposite side because of the greater quantity of blood passing through it Finally, pulsations and oscillometric readings distal to the fistula are almost invariably reduced Confirmatory evidence for the presence of an arteriovenous fistula can be obtained by demonstrating a high oxygen content in a sample of blood withdrawn from a vein above the level of the lesion

Differential Diagnosis

Traumatic Arterial Aneurysm An acquired arteriovenous fistula must be differentiated from several disorders prominent among which is arterial aneurysm of traumatic origin In the latter condition although a pulsating mass is present the associated local thrill is much shorter in duration than it is in an arteriovenous fistula Moreover the bruit is systolic in timing little or no sound being heard during diastole and is limited to the immediate vicinity of the lesion This is *in contrast with* an arteriovenous fistula in which the murmur is continous and is transmitted for some distance on either side along the course of the vessels

In the case of an arterial aneurysm arterial pulsations oscillometric readings and skin temperature are generally normal in the distal portion of the limb while in the proximal portion in the vicinity of the lesion there are no signs of dilated venous channels or raised skin temperature Furthermore *digital obliteration* of the aneurysm produces no changes *in heart rate or blood* pressure (negative Branham s bradycardiac sign) while examination of venous blood obtained from above the level of the lesion reveals a normal oxygen content All these findings differ from those observed with an arteriovenous aneurysm

If there is still some question regarding the diagnosis arteriography should be able to differentiate between the two conditions (Fig 41) In an arteriovenous

reduced Despite this, however the venous pressure is also high, due to the deterrent to the free movement of blood out of venous channels in this site offered by the high pressure existing in the collecting veins above the level of the fistula

Clinical Characteristics

The clinical picture of an arteriovenous fistula is generally much more characteristic than that which is associated with arterial aneurysm In all instances there is a history of trauma to an extremity followed by the appearance of a mass which may vary considerably in size (Fig 40)

Symptoms After the difficulties associated with the original injury have disappeared the patient may complain of pain locally as neighboring tissues particularly nervous elements are compressed by the distended sac At times he may experience a shaking throbbing or humming sensation in the limb As the condition progresses some dyspnea with effort and even nocturnal dyspnea may be experienced

Systemic Signs As already mentioned certain compensatory cardiovascular mechanisms come into play to combat the alterations produced by the secondary circulation These manifest themselves in the form of a rise in pulse rate and a widening of the pulse pressure due primarily to a fall in diastolic blood pressure Despite the marked augmentation in venous return central venous pressure remains normal until the heart begins to show signs of impaired efficiency When this occurs, the venous pressure will rise and associated typical findings of congestive heart failure will appear At this stage there may be x ray evidence of enlargement of the ventricular chambers due primarily to dilatation, and electrocardiographic changes indicating left heart strain

Information concerning the amount of blood that is passing through the fistula can be obtained by means of the following procedure (Branham's bradycardiac sign) With the patient lying down for about 15 minutes control blood pressure and heart rate readings are recorded Then the main artery above the level of the fistula is completely occluded by digital pressure this being confirmed by noting collapse of the mass and the absence of any bruit with auscultation With the pressure maintained, another set of readings is obtained

Depending upon the quantity of blood passing through the fistula the cardiovascular mechanisms called into play by the test may or may not be capable of coping with the altered situation With the communication closed the blood which ordinarily fills the secondary circuit must now be redistributed among other vascular beds In the presence of a small tract the excess quantity can generally be readily accommodated and hence there is little change in blood pressure or pulse rate If the fistula is large the resulting increase in the capacity of the arterial tree may not be adequate so that the vascular bed becomes overfilled with blood This situation produces an augmentation in venous return and a transient rise in blood pressure As a consequence of the latter response there will be stimulation of the aortic depressor nerve and endings in the carotid sinus This will be followed by peripheral dilatation due to an inhibitory action on the vasomotor center and a slowing of the heart rate via the vagus Both alterations tend to counteract the increase in blood pressure However such changes may not be

Congenital Arteriovenous Fistula An acquired arteriovenous fistula must also be differentiated from the congenital type (Chap XXIII) In the latter there is no history of trauma and the lesion has generally been present from birth or shortly thereafter However if its growth was slow it might not have become apparent until adolescence or later The typical findings of a thrill and bruit are usually not present In most instances the extremity in the case of a congenital arteriovenous fistula is longer than normal a finding which is not noted in an acquired arteriovenous fistula Signs of reduced arterial circulation to the foot or hand are much less prominent than in the acquired type Arteriography will generally visualize the great extent of the lesion and the presence of numerous connections between arteries and veins

TREATMENT

Almost all cases of traumatic arteriovenous fistula of the major vessels of the limb require surgical therapy since otherwise impaired function of the heart will eventually result On occasion spontaneous closure may occur following thrombosis and under these circumstances no other steps are necessary unless associated nerve lesions are present which require surgical intervention

An operation which has had considerable clinical trial is quadruple ligation The proximal and distal ends of the artery and vein are tied all openings into the sac are closed and the latter is removed However before such a procedure is carried out the state of the collateral circulation should be determined using the modified reactive hyperemia test (Chap II) In most cases the operation should be performed only if the local blood flow appears adequate when the fistula is closed by digital pressure Since in the presence of an arteriovenous fistula there is a persistent state of anoxia of the tissues distal to the lesion the stimulus to the growth of a collateral circulation is much greater than in the case of an arterial aneurysm Hence the problem of an adequate blood supply following operation is not as serious The optimum time for surgery is 4 to 8 months after the production of the fistula

When it is necessary to operate before an adequate collateral circulation has time to develop restorative procedures may be attempted followed by anti coagulant therapy Although repair of the artery would seem to be the most logical approach to the problem certain objections to this procedure exist First the possibility of subsequent thrombosis must be considered even when adequate anticoagulant therapy is used Second the surgeon may be misled by the seemingly normal appearance of the vessel wall when actually weaknesses are present which will manifest themselves as aneurysmal dilatations when exposed to a normal arterial blood pressure This is especially true in the case of high velocity missiles which tend to produce a shattering effect on adjoining tissues as well as direct trauma to the structures in the line of the bullet

In general then it appears to be safer to use a vein transplant to produce continuity of the lumen of the artery at the site of the removal of the fistula than to rely upon repair of the segment of vessel Furthermore in most instances the technical difficulties are much less with such an approach



Fig 41 Arteriography as a diagnostic aid in arterial and arteriovenous aneurysms A Brachial artery aneurysm B Popliteal artery aneurysm C Femoral arteriovenous aneurysm with contrast medium present in both artery and vein as well as sac

fistula, dye injected into the artery above the level of the lesion will rapidly be found in the large venous channels while very little will be present in the arterial tree in the distal portion of the limb In the arterial aneurysm the sac will generally be outlined (provided it is not filled with clot) and also the distal branches of the artery Little or no dye will be noted in the venous system At times a routine x ray may visualize a calcified rim in the case of the arterial aneurysm

dissection or manipulation of the main artery during a surgical procedure The response may occur even though the vessel itself is not directly traumatized Contusion of its wall almost invariably produces spasm Fractures particularly at the elbow joint or in the region of the knee joint are also predisposing factors as well as certain procedures utilized in their treatment including marked traction and tight casts

Pathogenesis The factors which maintain the artery in a state of spasm are a decrease in blood pressure in the vessel and active contraction of the circular muscular fibers in its wall The mechanism responsible for the latter response may be neurogenic, myogenic or both In the neurogenic type of arteriospasm the initiating factor is the traumatized or irritated segment of artery acting as a trigger mechanism to bring into play a reflex arc, which includes the sympathetic nervous system as the efferent arm Spasm occurs as a result of the increase in the number and intensity of the vasoconstrictor impulses reaching the involved vessel and its branches

Myogenic arteriospasm also follows irritation of an arterial segment However the exact mechanism responsible for the maintenance of this state is not clear although there is some support for the view that the contraction of the circular muscular fibers in the vessel wall represents a response of sensitized tissues to circulating vasopressor substances In contrast to neurogenic vasospasm myogenic [illegible]

[illegible] spasm are similar since in both cases they are due to the same mechanism a markedly reduced blood flow to the tissues supplied by the involved vessel The findings may resemble those observed with sudden organic occlusion of a comparable-sized artery except that the amount of pain and nerve involvement is less than would be anticipated on the basis of the extent of pallor of the skin Characteristically there is a decrease in cutaneous temperature at the level of the injury and distally The skin assumes a cadaveric appearance with cyanotic mottling in some areas as a result of trapping of blood Frequently neurologic signs are present such as wrist or foot drop paralysis of the smaller muscles of the hand or foot and a stocking glove type of anesthesia or hypesthesia The peripheral pulses become greatly reduced or even impalpable these changes being confirmed by markedly decreased or absent oscillometric readings

Spasm may follow different trends depending upon the underlying mechanism and the type of treatment instituted If neurogenic in type the signs and symptoms may disappear spontaneously or after removal of vasomotor tonus In some instances however progression to the point of gangrene may occur or the limb will show no trophic changes but remain cold and functionally impaired for many months

Myogenic vasospasm is almost always followed by a much more severe clinical picture In many instances complete and prolonged anoxia of tissues produces nutritional changes

Differential Diagnosis Neurogenic spasm can be distinguished from myogenic spasm by the fact that removal of vasomotor tonus generally causes immediate disappearance of symptoms and signs in the former while having little or no

Complications and Prognosis

The outlook in the untreated case of arteriovenous fistula depends upon its size and its effect upon the heart As has been stated if a considerable portion of the circulating blood volume passes through the communication eventually congestive heart failure will ensue If the fistula is small and some distance from the heart then the alterations in hemodynamics are generally minimal Under such circumstances the increase in circulating blood volume is sufficient to compensate for the existence of an ineffective secondary circuit while the greater work load placed on the heart is usually not enough to cause significant impairment of cardiac function Nevertheless, since bacteria may lodge and multiply at the site of a traumatic arteriovenous fistula even in the case of a small lesion of this type, surgical intervention is justified

Aside from systemic changes an arteriovenous fistula may be associated with a number of local complications Among these are chronic ulcers located in the distal portion of the limb particularly around the ankle These result from the chronic state of anoxia and the venous stasis due to the high venous pressure Because such lesions are surrounded by dilated blood vessels, it is not uncommon for profuse bleeding to occur after slight local trauma If the fistula involves the femoral or popliteal artery, intermittent claudication may be experienced in the legs due to a shunting of arterial blood through the communication into venous channels at the expense of muscle circulation

Following operation there should be no difficulties provided an adequate collateral circulation has been demonstrated In most instances the nutrition of the tissues distal to the fistula will immediately improve and the skin temperature will increase In some cases however after fistulectomy intermittent claudication easy fatigability and muscular atrophy may develop

Most of the systemic changes are reversible, if permanent cardiac damage has not been produced Generally symptoms and signs of congestive heart failure disappear soon after the operation Similarly the heart size electrocardiogram circulating blood volume and cardiac output return to normal

OTHER COMPLICATIONS OF INJURY TO ARTERIES

Trauma may also produce acute vasospasm thrombosis laceration and severance of an artery All of these can be considered to be vascular emergencies

Acute Vascular Spasm (Traumatic Vasospasm)

The most common complication of injury to vascular structures is spasm not only of the involved segment of vessel but frequently of the entire arterial bed in the extremity The response may last for hours or even days and because of the associated arterial inefficiency, serious and irreversible changes may occur in the skin nerves muscles and joints of the limb

Etiology Acute vascular spasm may result from a blunt blow to an extremity crushing injuries, a gunshot wound in the vicinity of vascular structures and

beneficial effect.[3] If relaxation does not occur in this period, the wound should be loosely closed, leaving a fine polyethylene tube in contact with the artery, for future installations of a 1% solution of papaverine at intervals until either circulation is restored or irreversible changes have occurred. Caffeine sulfate and Priscoline have also been used, but more successful results can be expected with papaverine.

Among other procedures which have been suggested for the treatment of myogenic spasm are periarterial sympathectomy by stripping of the adventitia, forcible stretching of the lumen of the vessel by injection of saline under pressure through a #17 needle, and transection of the contracted segment of vessel followed by end-to-end anastomosis if feasible. Unfortunately, *in most instances* these procedures have very little beneficial action. Still they should be tried if bathing the segment of vessel in vasodilators is ineffectual. In all instances the postoperative use of anticoagulants is indicated to minimize intra-arterial thrombosis.

Prognosis and Complications. The outlook in neurogenic arteriospasm *is good* provided measures to remove vasospasm are started early. However, if there is a *considerable delay* in initiating a therapeutic program, secondary thrombosis may take place; under these circumstances the prognosis is poor, with *gangrene and amputation* liable to result. Other relatively less serious complications are Volkmann's contracture and necrosis of muscles.

In most instances myogenic arteriospasm that can not be *removed after 8 to 10 hours* is *followed* by death of tissue, the *degree of involvement* depending upon the size of vessel *affected*. The responsible mechanism is secondary *thrombosis of* the involved arterial segment, *followed by propagation* of the process into the terminal branches of the arterial tree.

Traumatic Arterial Thrombosis

Pathogenesis. Traumatic arterial thrombosis may take place either in healthy vessels following severe injury or in diseased channels as a result of a lesser degree of damage. The etiologic factors are of two types. One is sudden direct injury to the artery by such agents as a fracture, a blow, a shell fragment, or a bullet causing destruction of the *normal* intimal layer but not affecting the continuity of the vessel. As a *consequence* there is a tendency for platelets and debris from the circulating blood to be *deposited on the* involved site, which acts as a focus for the production of a thrombus. The latter continues to propagate *until* complete occlusion of the vessel *at the point of trauma* occurs. Histologic examination of such a segment of artery generally reveals no signs of active arteritis or periarteritis.

The second and much more common cause *of arterial* damage resulting in *thrombosis* is moderate and indirect *pressure to the* exterior of the vessel, applied intermittently and transiently over a relatively long period of time until breakdown of the intima ensues. This is *followed* by the gradual growth of a clot to the point of obliteration of the lumen. In ...

... the first rib and behind the tendon of

effect in the latter However, it should be remembered that if neurogenic spasm has existed for a prolonged period of time before vasomotor control is eliminated the persistent anoxia may have produced permanent changes in nervous structures so that now sympathetic denervation no longer results in a complete reversal of the clinical picture

Differentiation between myogenic arteriospasm and sudden occlusion of an artery by an embolus is much more difficult and at times it can not be made until the vessel is exposed and examined Absence of a mass in the lumen and the findings of a markedly contracted artery would favor the diagnosis of myogenic vasospasm Clinically, the history of injury to the limb in the vicinity of the vessel *and the lack of any etiologic factor for the production of emboli would also tend to* support such an impression Removal of vasomotor tonus is of little diagnostic value, except when there is a considerable degree of superimposed vasospasm associated with embolism Under such circumstances the measure may be followed by some improvement in the symptoms and physical findings

Both types of acute vasospasm must also be distinguished from sudden severance of a main artery (p 304) The presence of a markedly reduced peripheral circulation is common to all three conditions and hence of little diagnostic value In the lower extremity, limitation of passive dorsiflexion of the foot in the absence of local pathology in the ankle joint, suggests acute interruption of the main artery (*plantar fixation sign*) rather than vasospasm A confirmatory sign is the sensation *of a markedly edematous calf muscle*

Treatment The treatment of neurogenic arteriospasm for the most part involves the temporary inhibition of all vasomotor control over the blood vessels in the involved limb This is accomplished through the use of repeated paravertebral sympathetic blocks continuous caudal anesthesia sympathetic blocking agents the intravenous and intra-arterial administration of papaverine oral whisky, and reflex vasodilatation Until these measures are effective, the extremity should be covered with a boot of surgical cotton to preserve its natural heat

Therapy is frequently unsuccessful in myogenic arteriospasm Attention should be directed first to the precipitating agent If a fracture is responsible then it should be reduced so as to remove pressure of the bony fragments on the irritable arterial tree Compression caused by traumatized tissues or blood clot should also be relieved surgically and the extremity splinted in such a manner that further pressure is prevented At the same time, attempts should be made to remove vasomotor tonus but generally the ineffectiveness of such an approach reveals *the true nature of the condition*

Since continuation of myogenic vasospasm is almost invariably associated with death of tissue failure of previous procedures makes it imperative to resort to more heroic measures These include surgical exposure of the artery with special care to avoid contact of the vessel with any metal instrument Warm saline dressings are then inserted into the wound and if this has no effect the local application of vasodilating agents should be attempted in the hope that now they will be more successful than was their previous intravenous or intra-arterial administration In this regard, bathing the entire segment of involved artery in a warm 2 5% solution of papaverine sulfate for 10 to 15 minutes may have a

hemorrhage will be external On the other hand if the bleeding takes place into the surrounding soft tissues a hematoma will form which in turn may cause compression and even complete occlusion of the involved vessel when the pressure of the extravasated blood becomes greater than that within the artery Under such circumstances hemorrhage will cease At times if the concomitant vein is also traumatized an arteriovenous fistula will result

Clinical Manifestations The clinical picture associated with laceration of a main artery followed by bleeding into the tissues is related to the ensuing state of shock due to loss of blood and to the local anoxia of the structures in the involved limb If complete severance of the artery has occurred or if this is only incomplete but the resulting hematoma has produced occlusion of the vessel by compression the extremity will manifest all the signs of complete obstruction of the local circulation (See *Arterial Embolism* Chap X)

Treatment The treatment of laceration or severance of a main artery has a twofold aim One is to combat the state of shock and to restore the normal blood volume by preventing further bleeding and replacing the lost blood The other is to re-establish the local circulation in the involved limb and thus maintain the viability of the tissues

The treatment of the local bleeding will depend upon the size of the affected vessel and its location Under some circumstances hemorrhage from a small artery can be controlled by digital pressure or by a firm pad or bandage but if this is not successful actual clamping of the cut ends may be required Hemorrhage from a large vessel like the femoral or axillary artery generally necessitates the use of a tourniquet applied around the extremity However this type of obstruction should not be permitted to remain on the limb for more than an hour for the acute anoxia may cause irreversible changes in the various structures Furthermore it must be remembered that a tourniquet not only occludes the involved artery but also all collateral vessels Although the latter may not be enough to nourish the limb the fact that blood is flowing through them may impede the tendency toward thrombosis frequently present in the ...

Just as important as the prevention of fı ... of blood volume to a normal level in an atterr ... his can be accomplished by intravenous transfusions or more rapidly by the intra-arterial route[1] The latter procedure has the advantage of making the blood immediately available for distribution throughout the systemic circulation including the brain at the same time that the coronary circulation is benefitted It also prevents too great a load from being placed suddenly on a heart in a poor state of nutrition

Once the state of shock is controlled attention should be directed to the local condition in the limb The area is exposed surgically and attempts made to restore the continuity of the lacerated artery If the involvement is minimal all that may be necessary is removal of the torn segment and an end to end anastomosis Such a situation occurs if the lesion has been produced by a sharp instrument However lacerations associated with a gun shot wound or blunt trauma are generally more extensive and jagged and reunion of the ... difficult At times ...

the scalenus anticus muscle, and hence it is susceptible to injury by a hypertrophied muscle or a large cervical rib exerting intermittent and partial compression (Chap XX) The basis for the relatively frequent thrombosis of the popliteal artery from indirect trauma is probably the fact that this vessel is firmly fixed to the oblique ligament of the knee joint As a result, it may be damaged by the repeated contractions of the surrounding muscles as it courses through the fibromuscular canal at the level of the upper border of the femoral condyles The femoral artery in its passage through the adductor canal is likewise vulnerable to such forces

Clinical Characteristics The severity of the symptoms and signs will depend upon the etiologic agent If the occlusion develops rapidly, then the clinical picture will mimic an arterial embolism, while in the presence of a slow forming obstruction produced by intermittently applied mild trauma, the changes will be similar in most respects to those observed in arterial thrombosis due to a chronic disease process (Chap X) The differentiating point for both types of traumatic arterial thrombosis is the antecedent history of some kind of injury sustained in the vicinity of the involved vessel

Treatment Therapy in acute arterial thrombosis consists first of eliminating the precipitating cause such as a hematoma producing pressure on the vessel or injured tissues having a similar effect, particularly fragments of bone At the same time attempts should be made to remove the thrombus and to inhibit vasomotor tonus, as through continuous spinal or caudal anesthesia in the case of involvement of vessels in the lower extremity Heparin and the longer acting anticoagulants should be given in order to prevent propagation of the thrombus or its recurrence if it has been removed Later if arteriography demonstrates a segmental type of thrombosis, the involved portion should be replaced by a vein transplant

In the slow forming type of arterial thrombosis produced by indirect trauma, again attempts should be made to remove the etiologic factor if possible Once complete occlusion has occurred it is questionable as to whether anticoagulants will have any effect In the case of the lower extremity, excision of the thrombosed segment and substitution of a vein transplant is indicated, while in the case of the upper extremity such an approach is generally not warranted

Laceration or Severance of a Main Artery

Traumatic laceration or complete division of a main artery may result in marked anoxia of tissues as well as the serious complication of hemorrhage The latter is noted much more often after total severance since under these circumstances arterial contraction is not as effective nor is the possibility of the occurrence of extravascular clotting as great The lesions may be produced either by sharp instruments such as a razor a knife or an ice pick, by bullets by blunt objects or by fragments of fractured bone The vessels generally affected are those close to the surface of the limb and not well protected by bony structures, as for example, the femoral, the brachial and the radial arteries

Pathogenesis Two types of response occur after injury to the vessel If the wound has caused penetration of the skin and other overlying structures the

CHAPTER

XVIII VASCULAR ENTITIES PRODUCED BY TRAUMA OR NOXIOUS AGENTS

(*Continued*)

2. POSTTRAUMATIC PAINFUL LESIONS

Trauma to nonvascular tissues of an extremity may be responsible for several vascular conditions characterized by pain and varying degrees of vasomotor imbalance The better known of these are causalgia causalgic states and posttraumatic vasomotor disorders Although such syndromes have a number of features in common enough clinical differences exist to make it advisable to deal with them as separate entities

CAUSALGIA

Through common usage the term causalgia (major causalgia) refers to the sequelae which may follow peripheral nerve injury in the upper and lower extremities The damage may vary in degree from minor involvement of the nervous tissue insufficient to cause sensory or motor changes to destruction of the entire nerve trunk[8]

Pathogenesis

A number of theories have been proposed to explain the changes in causalgia but none has received sufficient experimental or clinical support to be seriously considered Among those suggested are infection associated with penetrating wounds an irritable focus resulting from the trauma setting up an exaggerated state of activity in the spinal cord and a short-circuiting effect in the areas of injured peripheral nerve permitting direct stimulation of adjacent sensory afferent fibers by the continuous flow of sympathetic impulses[7]

Clinical Characteristics

Symptoms The clinical picture of causalgia is very typical and readily identified The most characteristic point is the agonizing burning and constant pain generally limited to the distal portion of the involved limb This may be expe

wall results in a defect which can only be bridged by a vein transplant In other instances the undesirable alternative of ligating the cut ends of the vessel may have to be carried out Of interest in this regard is the incidence of gangrene resulting from such a procedure subclavian and axillary, 9 per cent, brachial 3 per cent, radial or ulnar, 0 per cent, external iliac, 13 per cent femoral, above the origin of the deep femoral, 21 per cent, femoral below the origin of the deep femoral, 10 per cent popliteal, 37 per cent, and posterior tibial or anterior tibial, 0 per cent[1] Whenever the continuity of the artery has been re-established, it is necessary to use anticoagulants to prevent intravascular clotting

Prognosis The outlook depends upon the rapidity with which the blood volume has been restored the size and importance of the vessel involved and the resultant state of local circulation If permanent damage to brain tissue had occurred during a prolonged period of hypotension, the prognosis is grave Similarly, if the only course left to control the hemorrhage is arterial ligation there is the possibility of subsequent gangrene, which may also follow an unsuccessful attempt to re-establish the continuity of the vessel In other instances the rapid formation of an adequate collateral circulation may be sufficient to maintain the distal tissues in a state of viability

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Prognosis

Without treatment the prognosis in causalgia is poor On occasion spontaneous repair of the injured nerve may result in a reduction or even disappearance of the pain In other instances the symptoms tend to disappear slowly after one or two years In most cases however, they persist unabated in severity leading to drug addiction mental deterioration, and at times even suicide Besides the effect on morale and emotional stability there may be permanent damage of the skin and muscles and physical incapacity of the limb On the other hand with proper therapy instituted early enough the condition can be controlled and the pain eliminated Then function can be restored through physical therapy

CAUSALGIC STATES (MINOR CAUSALGIA)

The clinical entities falling into the category of causalgic states may resemble major causalgia In fact in the opinion of some workers there is no real distinction between the two groups other than a matter of degree of severity a case of major causalgia becoming one of minor causalgia as improvement occurs The most common of the disorders falling into the category of minor causalgia are postamputation fingers syndrome traumatic neuralgia and phantom limb[1]

Clinical Entities

Postamputation Fingers Syndrome In this condition the stumps manifest a cyanotic rubor and are tender cold and sensitive to a low environmental temperature There may be marked hyperesthesia and burning pain locally The explanation for the onset of the changes following amputation of one finger and not after another is not clear

Traumatic Neuralgia In this state hyperalgesia is the main complaint The fact that there is no spontaneous burning pain helps to differentiate the condition from true causalgia

Phantom Limb This term is used to designate the illusion of the existence of a limb after amputation Frequently the patient experiences the pain that had previously been present in the gangrenous extremity and is even able to localize it to the offending digits This symptom may be so severe as to be incapacitating It may take the form of a boring pain in the bones or a sense of tearing pressing or burning in the toes Slight trauma to the stump nervous tension pain elsewhere exposure to cold and changes in weather may all aggravate the complaints There may be signs of sympathetic hypertonus noted in the stump such as coldness and hyperhidrosis

The cause of the syndrome is not clear but it may be due to abnormal stimulation of afferent pathways in the large mixed nerves cut in the course of the operation The immediate etiologic agents may be inflammation compression laceration or a neuroma of the involved portion of nerve

In the treatment of phantom limb therefore the first step should be prophylaxis This involves special care at the time of surgery to prevent unneces

nenced within several hours after injury or its onset may be delayed for weeks Many factors appear to aggravate the symptom Among these are extremes of environmental temperature, loud or unexpected noises, laughing, defecation and urination, jarring of the bed, and use of the affected limb or placing it in dependency Because of the marked hyperesthesia, mere touching or tapping the involved structures increases the pain Frequently the patient finds relief by keeping the extremity immersed in water At all times he guards it against any external stimulus

Signs Associated with the pain are findings of sympathetic imbalance Early in the disorder these may occasionally take the form of vasodilatation, resulting in a warm dry, and pink limb[3] However, much more frequent signs are increased sympathetic tonus the extremity being cold blue or red, and wet

Nutritional changes appear early in the disease Among these are a glossy appearance, fissuring and atrophy of the skin of the involved limb The digits are generally tapering smooth, and almost devoid of wrinkles There is usually x ray evidence of atrophy of bone, varying from slight generalized loss of density to advanced osteoporosis The muscles may undergo fibrous changes which cause them to be almost immovable, while the small joints become stiffened and ankylosed

TREATMENT

Treatment of causalgia must be undertaken as soon as the diagnosis is made, in order to forestall irreversible changes

Sympathetic Denervation Temporary or permanent removal of sympathetic control appears to be most effective in minimizing or even eliminating the pain of causalgia Repeated sympathetic blocks with procaine may in some instances have a relatively permanent effect provided the treatment is carried out daily over a period of time and there is an increasing period of benefit with each subsequent one, beyond the anticipated duration of sympathetic anesthesia[2]

Sympathetic blocking agents may also produce some relief For this purpose daily intravenous or intramuscular injections of Etamon in doses of 400–5000 mg have been used[1] The oral administration of Priscoline 25 mg, Hydergine 0 5 mg and Dibenzyline 10 mg several times a day is also worthwhile (For pharmacologic action of these drugs, see *Vasodilator Drugs* Chap XXX)

Sympathectomy has been given an extensive clinical trial in causalgia It is advisable in each instance to do a preliminary paravertebral sympathetic block, and only if the pain is temporarily alleviated by such a procedure should permanent denervation be carried out If the results are not clear-cut, it is questionable whether the operation is warranted

Physical Methods Although there is no doubt that disuse plays a prominent role in the clinical picture attempts to counteract this through the use of physical therapy are generally disappointing The pain and hyperesthesia are so great that the patient will not submit to massage or manipulation Similarly heat will aggravate the symptoms However all these procedures should be utilized vigorously once the pain is controlled Occupational therapy is of value as a supplementary measure

portant part in the pathogenesis of the condition This factor alone may be responsible for such changes as a reduction in blood flow coldness cyanosis, hyperhidrosis edema and osteoporosis changes which are generally considered also to be part of the clinical picture of posttraumatic vasomotor disorders As a consequence it is often difficult to evaluate the relative roles of the trauma and the reflexes initiated by it on the one hand and of the resultant disuse on the other[4]

Clinical Characteristics

Symptoms One of the most important complaints in posttraumatic vasomotor disorders is pain in the involved limb often far out of proportion to that anticipated on the basis of the original injury In the case of the lower extremity this symptom is primarily experienced on weight bearing or with other physical activity necessitating movement of the injured limb Though commonly described as an aching sensation it may also be throbbing or burning in character However the complaint of burning is much less frequently observed than in major causalgia The pain is usually severe enough so that attempts to persuade the patient to resume normal use of the involved extremity are in most instances futile

There are several other possible symptoms Among these are a subjective sense of coldness of the limb sensitivity to a cool or cold environment stiffness and numbness of the affected digits and tenderness to superficial and deep pressure

Signs A common finding is muscle weakness at times almost to the extent of paralysis of the limb[4] Associated with this alteration muscle atrophy and stiffness of the joints may be evident There may also be a variable degree of pitting or nonpitting edema which does not respond readily to prolonged elevation of the limb (Fig 42A and C and Fig 43A) Other signs of vasomotor imbalance may be noted such as cyanosis coldness and hyperhidrosis In general one of these is exhibited out of proportion to the others[4] and not all are necessarily present in each patient

X ray changes in the bone are relatively frequent and striking and may be noticed within several days after the initial injury The earliest manifestations are found in the small bones like the carpal and tarsal bones the heads of the metacarpal and metatarsal bones and the phalanges while the long bones are spared Initially the alterations consist of irregular rarefaction of the spongiosa giving an appearance of mottling As the process progresses there is a generalized loss of density so that the tissues become radiolucent and resemble osteoporosis from other cause

Differential Diagnosis

Posttraumatic vasomotor disorders must be differentiated from several conditions Among these are causalgia causalgic states malingering traumatic neurosis and a variety of entities which manifest vasospasm as part of their clinical picture (Table 5 p 116) Because of the bony changes one must also consider atrophy of disuse and senile osteoporosis Some of the more important of these entities will be discussed below

The history of a penetrating wound in the vicinity of a major nerve trunk in

sary injury to large nerve trunks, all incisions through such structures being made with a sharp knife Once the condition has developed it may be necessary to utilize narcotics if the symptoms are severe In some instances even lobotomy has been performed to control the condition Amputation of neuromas usually fails to give relief However, temporary sympathetic denervation as through repeated paravertebral sympathetic blocks or the use of sympathetic blocking agents, may be helpful In many instances the condition will disappear spontaneously several months after amputation In others it may be present at intervals and in gradually diminishing severity for many years Reassurance of the patient is of great value in controlling the symptoms

POSTTRAUMATIC VASOMOTOR DISORDERS

General Considerations

In some cases of trauma to a limb there are superimposed upon the changes due to injury certain findings which can be accounted for only on the assumption that some reflex disorder has been initiated by the local tissue damage This clinical entity has been the subject of gradually increasing study and interest since 1900 when Sudeck[7] first described a condition of acute atrophy of bone following inflammatory processes The numerous terms used to describe this clinical entity indicate not only that widespread disturbances are present but that there is a lack of agreement as to what constitutes the primary characteristic change Because vasomotor abnormalities are constant findings the broad term posttraumatic vasomotor disorders appears to be appropriate[4] Among other designations which have been used are Sudeck s atrophy, acute atrophy of bone posttraumatic osteoporosis, posttraumatic painful osteoporosis, traumatic arthritis peripheral trophoneurosis reflex nervous dystrophy, reflex sympathetic dystrophy traumatic angiospasm, posttraumatic dystrophy posttraumatic edema and chronic traumatic edema

Pathogenesis

It is generally accepted that the primary mechanism responsible for the changes observed in posttraumatic vasomotor disorders is some type of reflex disturbance initiated by the local injury and dependent upon a reflex arc which includes the components of the sympathetic nervous system Various theories have been proposed to explain the pathogenesis but no definite proof has been obtained to verify the correctness of any of them

The precipitating factor can be a number of different types of trauma Among these are such minor involvements as a slight soft tissue injury, a burn frostbite and a sprain or such serious conditions as a crushing injury and a simple or compound fracture of small and large bones Low grade chronic infections may also produce the disease There appears to be little relationship between the degree of initiating trauma and the severity of the posttraumatic vasomotor disorder In fact a severe injury is not ordinarily a precipitating cause

There is little question that the associated disuse of the limb brought about by the original injury or by fear of eliciting pain with movement plays an im

associated with a diffuse type of bony atrophy which comes on slowly and improves with the assumption of physical activity In contrast the osteoporosis of posttraumatic vasomotor disorders occurs soon after the inciting injury and disappears very gradually even after complete rehabilitation The existence of vasospasm is of little value as a diagnostic point, since this response may also be noted in both conditions

Malingering following a minor injury must be considered in the differential diagnosis particularly early in the condition A hard traumatic edema of the

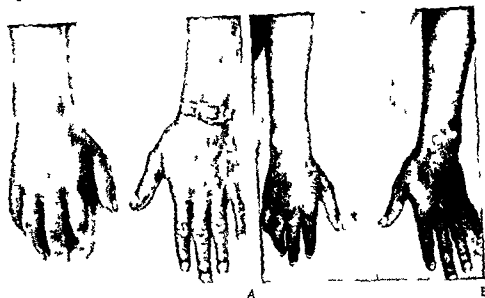


Fig 43 Posttraumatic vasomotor disorders A Marked edema of right hand following minor injury to elbow B Complete disappearance of swelling and return of function after several weeks of intensive physical and occupational therapy (From H B Shumacker Jr and D I Abramson Posttraumatic vasomotor disorders with particular reference to late manifestations and treatment *Surg Gynec & Obst 88* 417 1949 by permission of *Surgery Gynecology and Obstetrics* Copyright Dec 194, [April 1949] The Franklin H Martin Memorial Foundation)

hand artificially produced by a constricting band may resemble the swelling of posttraumatic vasomotor disorders Although the constriction may not be visible to the naked eye at the time of examination an infrared photograph will generally show the site of the obstruction as a ring of subcapillary extravasations [8]

Hysterical disability following an injury to the hand or foot may mimic posttraumatic vasomotor disorders closely The limb may be subjectively cold and objectively cold and cyanosed [3] Motor power is generally markedly impaired the skin being soft and shiny Frank swelling may also be present

In contrast with the signs in posttraumatic vasomotor disorders there are certain findings which suggest a functional origin Among these are normal electrical reactions of the muscles a typical stocking glove type of anesthesia and absence of appreciable wasting of muscles Of further interest is the fact that if the patient is asked to perform a certain movement the forced effort results in either

the limb and the presence of severe burning pain are the cardinal points in the differential diagnosis of causalgia In contrast, in posttraumatic vasomotor disorders, the initiating trauma is generally mild in type, while peripheral nerves are not involved in the injury Although there are signs of increased vasomotor tonus

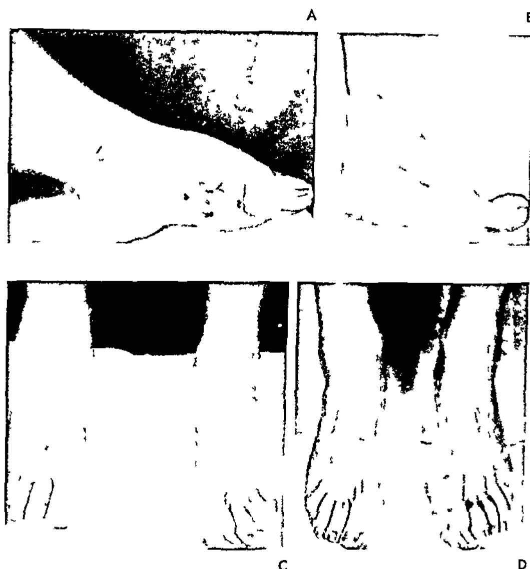


Fig 42 Posttraumatic vasomotor disorders A Massive edema of left foot and ulceration at site of original trauma resistant to conservative treatment B Same limb following lumbar sympathectomy showing disappearance of swelling and healing of lesion C Edema of right foot following a trivial shell fragment injury to ankle D Complete subsidence of swelling after intensive active exercise and physical therapy (From H B Shumacker Jr and D I Abramson Posttraumatic vasomotor disorders with particular reference to late manifestations and treatment *Surg Gynec & Obst 88* 417 1949 by permission of *Surgery, Gynecology and Obstetrics* Copyright Dec 1943 [April 1949] The Franklin H Martin Memorial Foundation)

and trophic changes in both, spotty osteoporosis and edema are much more common findings in posttraumatic vasomotor disorders than in causalgia

Atrophy of disuse may also be mistaken for posttraumatic vasomotor disorders However, there is no history of trauma or pain in this state Furthermore it is

fact that only through a correct gait are all muscles used in a manner which causes strengthening and improvement in tone In some instances it may be necessary for the patient to become ambulatory by first walking in a pool since the buoyancy of the water minimizes the pain experienced when the weight of the body is placed on the involved limb

In addition to the above measures considerable benefit can be obtained through gentle massage and directed active and resisted exercise of all the weak muscles The physical therapist should outline the program but the patient must be impressed with the view that it is his responsibility alone to carry it out In most instances the appearance of some improvement which almost invariably occurs after a short period of intensive physical therapy acts as a potent stimulus to the patient to continue faithful adherence to treatment Once this stage is reached the rate of relief of symptoms is accelerated (Fig 4 C and D and Fig 4,) An increase in muscle power is generally noted as well as an alleviation of vasomotor disturbances Almost invariably the limb which was previously cold wet, and cyanotic becomes warmer drier and normal in color

Neuropsychiatric Approach In some of the patients in whom physical therapy and active exercise have produced no therapeutic effect the underlying mechanism may respond to psychiatric measures particularly suggestive therapy under Amytal narco is or hypnosis

Sympathetic Denervation Certain patients resistant to other types of treatment may respond very well to sympathetic denervation In some instances repeated paravertebral sympathetic blocks may *cause steady improvement* in the clinical picture producing a diminution of the coldness hyperhidrosis edema and cyanosis Pain is apparently not a prominent feature in those patients who are benefitted by the blocks[4] Sympathectomy appears to be of some value in controlling or eliminating pain on weight bearing and signs of excessive sympathetic activity Chronic ulcers also heal much more rapidly after such an operation (Fig 42A and B) The effect on edema is variable ranging from rapid disappearance of massive swelling (Fig 4 B) to little improvement In all cases the therapeutic effects of sympathectomy are enhanced by the postoperative use of vigorous active exercises As a result of the reduction in pain following the operation movements of the involved parts are more readily attempted and carried out by the patient

Prognosis

There is little doubt that the longer the condition is left untreated the less is the possibility of eventual control regardless of the therapeutic approach After a period of disuse changes take place which are exceedingly difficult to reverse[4] Among these are osteoporosis muscle atrophy and the various mental attitudes already mentioned The latter may be due to fear of discomfort or to some motivation to prolong the disability such as a desire for compensation other rewards of invalidism and avoidance of duty in the case of an injured soldier However if the patient has the determination to get well and if the changes due to disuse are not as yet permanent little difficulty should be encountered in rehabilitating him and returning him to a normal state of physical activity On occasion the

a gross tremor or little or no motion of the part. This is the result of contraction not only of the muscles ordinarily utilized but also of their antagonists.[4] Another diagnostic point is that rarely is improvement noted with physical methods of treatment alone, while many patients make rapid progress when psychotherapeutic procedures, in the form of explanation, persuasion and suggestion, are simultaneously utilized with other approaches.

Treatment

Prophylaxis

The treatment of posttraumatic vasomotor disorders is first prophylactic, i.e. proper care of local lesions which could conceivably act as a focus of irritation and thus precipitate such a condition. This step involves debridement of wounds, removal of foreign bodies, surgical treatment of torn muscles, tendons, and ligaments, evacuation of hematomas and appropriate immobilization of fractures. At the same time steps should be taken to control the pain associated with the original lesion. In this regard it may be advisable to infiltrate hematomas in acute strain with procaine or even to produce a regional nerve block. Finally, the alleviation of fear and anxiety and reassurance of the patient concerning the injury may reduce the possibility of a conscious or subconscious prolongation of a painful syndrome.[2]

Active Therapy

When it becomes apparent that some profound vasomotor disorder is superimposed upon the original injury, then intensive therapy should be instituted at once. Otherwise the patient soon begins to assume the attitude and behavior of the chronic invalid and regards eventual recovery as hopeless.

Physical and Occupational Therapy. Early in the treatment measures should be instituted to encourage active exercise. It is advisable to explain their purpose to the patient, stressing the fact that a vicious cycle has been set up which would result in continued difficulty so long as the limb is not used.

If edema is present, attempts should be made to control this before beginning any other procedures. Under such circumstances the patient is placed at complete bed rest with the extremity elevated until the swelling has disappeared. If it recurs on resumption of activity, then some type of elastic support should be used to prevent this. At the same time physical activity is temporarily reduced to minimize the return of the edema.

If the patient is confined to bed when first seen, efforts should be made to have him become ambulatory again as rapidly as possible. It may be necessary for him to utilize crutches or a cane at the beginning, but these should be discarded as soon as practicable. Since at first the patient tends to walk timidly, favoring the affected limb, careful attention must be paid early in the reconditioning program to the acquisition of a normal stance and gait. The patient should be made to understand that more benefit is derived from walking a short distance properly than a long distance improperly.[4] Emphasis must be placed on the

CHAPTER

XIX. VASCULAR ENTITIES PRODUCED BY TRAUMA OR NOXIOUS AGENTS

(Continued)

3 CONDITIONS ARISING FROM COLD INJURY

Exposure of tissues to a low environmental temperature is the main cause of such vascular diseases as trench foot immersion foot the ordinary type of frost bite high altitude frostbite and chilblains

TRENCH FOOT AND IMMERSION FOOT

Since the pathologic changes and many of the clinical characteristics in trench foot and immersion foot are similar it has been considered desirable to discuss the two conditions together pointing out differences where they exist Both are neurovascular entities generally affecting the lower extremities particularly the feet As a result of the great number of soldiers and sailors who were exposed to prolonged periods of cold and dampness in World War II and the Korean War our knowledge of trench foot and immersion foot as well as of allied conditions has been considerably enhanced

Etiologic Factors

Trench Foot The most [illegible]

a [illegible]

A[illegible] position assumed in a foxhole which invariably places pressure on the popliteal space and therefore impedes venous return and to a lesser degree arterial inflow Dependency and immobility of the lower extremities together with the constricting effect of shoes or clothing also play a role Contributing factors are lack of acclimatization to cold insufficient sleep and underfed [illegible]

[illegible] ranges around 0 C

(3 [illegible] low temperatures required to produce frostbite (much below freezing) In trench foot however the detrimental effect of the cold is markedly enhanced by the associated moisture since water has a high capacity

condition may subside within several weeks without treatment, especially in the mild type If it lasts for a year or longer and then improves spontaneously, generally there is some residual disability such as joint contracture, stiffness and resultant deformity

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in a state of vasoconstriction Later organized thrombi are observed in both small arteries (Fig 44) and veins in some of which there may be signs of recanalization

The muscles and nervous structures also show signs of involvement Initially, degeneration necrosis and cellulitis may be noted in the muscles but no atrophy [7] Subsequently there is extensive atrophy with replacement by fibrous tissue At first

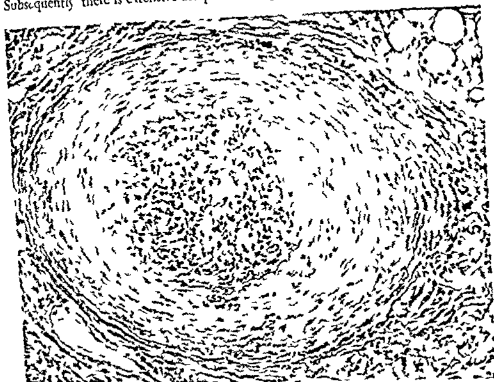


FIG 44 Vascular changes noted in trench foot Obliteration of lumen of an artery in a late case with rupture of the inner elastic membrane and scarring of *media* and adventitia Hematoxylin and eosin stain × 157 (Reproduced through the courtesy of N B Friedman The pathology of trench foot *Am J Path* 21 387 1945)

the nerves in the involved sites are swollen and edematous with areas of degeneration of axis cylinder and myelin especially in the distal portions [7] Later the nerves in regions of gangrene and cellulitis show signs of severe damage with edema of nerve bundles and separation of fibers

Immersion Foot In this condition biopsy studies [17] have revealed histologic changes in the tissues of the involved limb consisting of atrophy and thinning of the epidermis intense fibrosis and deposition of collagen around the nerve endings and subcutaneous blood vessels and infiltration and separation of muscle fibril by a network of scar tissue

CLINICAL CHARACTERISTICS

Clinically trench foot and immersion foot can be divided into several stages, depending upon the type of existing circulatory change

for absorbing heat and facilitating transmission of cold to the tissues However at no time are they actually frozen

Immersion Foot This condition is the seagoing counterpart of trench foot It is found in survivors of shipwrecks who are compelled to sit in a crowded open life boat or raft for many hours, with their wet feet dependent and immobile A difference between immersion foot and trench foot is that men in a crowded boat do not have the opportunity to walk that soldiers have, and, as a result, there is less chance for the anesthetic feet to become traumatized Accordingly, gangrene is less frequently seen in immersion foot *However, as a result of maceration of the* skin by sea water, secondary infection of the soft parts may occur The associated malnutrition and lowered general vitality due to physical exhaustion contribute to the latter possibility

Pathogenesis

The mechanisms responsible for trench foot and immersion foot are not clearly understood One of the views offered is that the cold leads to vasoconstriction followed by anoxia the latter in turn produces damage to capillary endothelial walls followed by transudation into tissue spaces and the formation of edema At the same time there is a concentration of the blood which is conducive to local thrombosis It is believed that the nerves are directly affected by the ischemia while destruction of the muscles probably follows loss of their nerve and blood supply

More obvious in immersion foot is the hyperemic state which often occurs suddenly after warmth applied to the body has overcome the vasoconstriction The excessive vasodilatation may be due either to an inflammatory response to cold to direct damage to the vessel wall particularly of the capillaries or to vasomotor paralysis as a result of interruption of vasoconstrictor fibers in peripheral nerves[1]

The rise in cutaneous temperature in the hyperemic state contributes to an *elevation of the metabolic needs of the tissues However since the circulatory* mechanisms hampered by the previous exposure to cold can not cope with the increased demands the already existing anoxia of tissues is exaggerated This factor is partly responsible for the appearance of nutritional disturbances In several weeks the state of excessive vasodilatation subsides and the circulation returns to normal Most of the cooling of the skin is probably due to lessening of the inflammatory process although an increase in intrinsic arteriolar tonus may also play a role

Pathology

Trench Foot The changes in the skin in this condition consist of foci of inter cellular edema the formation of vacuolated edematous cells and in the more severe cases necrosis of the superficial layers with degeneration and necrosis of the collagen of the dermis[7]

The changes in the vascular tree are marked Initially the capillaries and the venules in the papillary loops and the subpapillary venous plexus are widely dilated with extravasated red blood cells surrounding them At the same time these vessels may contain agglutinative erythrocytic thrombi The large arteries generally are



Fig 45 Nutritional disturbances in trench foot A Characteristic rigidity of toes B Superficial area of ne… C Similar lesions on ventral surface D … Necrosis of great toe and swelling of oth… oval of necrotic tissue with healing of operative site H and I Extensive gangrene of both feet (All photographs except C from D I Abramson D Lerner H B Shumacker Jr and F K Hick Clinical picture and treatment of the later stage of trench foot Am Heart J 32 5 1946)

Prehyperemic Stage In trench foot, during the period of exposure, the soldier first begins to notice an uncomfortable sensation of coldness of the feet followed by numbness and aching[1] There may also be temporary tingling and mild aching or cramping pain in the arches and sole of the feet Aside from some difficulty in walking little discomfort is present The patient with immersion foot may complain of heaviness of the feet, numbness, and insensitivity to pain touch and temperature

Examination during the prehyperemic stage of both disorders generally reveals the involved foot to be red initially and later waxy white Mottled cyanosis may also be present A stocking glove type of hypesthesia or anesthesia may be noted Pulsations in large vessels are reduced or even absent because of vasospasm On occasion the changes suggest the presence of impending nutritional disturbance which is not always borne out by subsequent events The prehyperemic or ischemic stage generally lasts for several hours

Hyperemic Stage Recovery probably takes place in two other phases, the first being one of intense vasodilatation which may last from 6 to 10 weeks[16 17] This develops soon after the limbs are removed from the cold wet environment Typically, the pulsations in the main arteries are bounding and the feet are red hot and dry There may also be petechial hemorrhages due to ruptured capillaries gross edema and vesicles filled with straw-colored fluid or extravasated blood Parts of the limb may become black as a result of superficial gangrene (Fig 45)

Sensory disturbances are frequently noted in the hyperemic stage[17] Tingling in the toes is felt early and may increase in severity The affected limbs may ache and throb and later in this phase there may be shooting pains All the symptoms are exaggerated during and after exercise, on placing the feet in dependency and on exposing them to extremes of temperature Associated with these complaints are loss of sensation to pin prick and deep pressure and absence of vibration sense perception, especially in the great toes Muscles whose points of nerve entry are within the cooled areas may show weakness and later wasting and impaired electric responses[17] Gradually all of the symptoms begin to subside with the rubor slowly fading to a waxy pallor or a normal color and the swelling decreasing to be followed by fine wrinkling of the skin

Posthyperemic Stage The second or posthyperemic stage of recovery lasts for weeks or months after vasodilatation has subsided In this period the swelling and blisters disappear as well as the high cutaneous temperature the latter being replaced in many instances by coldness of the feet and a marked sensitivity to cold Increased sweating instead of dryness of the skin is now present This response is noted both on exposure to a cold as well as to a warm environment with the result that the patient frequently complains that his socks rapidly become soaked even after mild exercise With an increase in walking and the use of normal footwear blisters and swelling may recur By this time the feet especially the toes may have become rigid and pain is experienced when ambulation is attempted (Fig 46) Such findings may persist for many months after exposure and are probably related to the histologic changes already mentioned There is little question that in part the weakness and deformities of the feet are also due to disuse The latter is frequently a prominent factor in both trench foot and

and loss of toes as a result of gangrene In many instances the gait may not be normal for as long as a year after exposure The patients tend to walk on their heel or the lateral edge of the feet or they keep the toes extended so that the digits do not participate in weight bearing or propulsion Hyperhidrosis and swelling of the feet are frequently noted during hot weather

TREATMENT

Prophylaxis The first therapeutic approach to trench foot is its prevention This involves measures which will conserve body heat and reduce prolonged exposure of the feet to moisture coldness and other factors that decrease peripheral circulation Various types of footwear have been suggested to keep the feet warm and d y but thus far none has proved entirely satisfactory It is not difficult to stop water from reaching the foot from the outside through the use of loose fitting waterproof or water resistant boots However the great disadvantage of this type of footwear is that it must be made of some type of rubber composition which generally prevents elimination of the moisture produced by sweating As a result there will soon be saturation of the sock and exposure of the foot to dampness a situation which is no different from that which occurs when the limb is kept wet by mud and rain

Recently attempts have been made to use an insulated shoe which retains body heat effectively This has been found satisfactory in keeping the foot actually hot so long as the soldier is able to walk for about 10 minutes each hour Unfortunately this is frequently not possible under present conditions of warfare and consequently the limb will cool down and become wet as a result of the factors already discus ed

There are other measures which may reduce the possibility of acquiring trench foot The soldier should avoid a cramped position or immobility for any period of time He should attempt to elevate his feet at intervals and move around even in the small limits of a trench or foxhole He should frequently inspect his feet and massage them in order to re-establish an adequate circulation All types of clothing which constrict the circulation should be removed and the upper part of the body should be kept warm and dry If possible socks should be changed frequently

Early Treatment The active treatment of trench foot or immersion foot should be directed at preventing first an increase in metabolism of the tissues present during the hyperemic stage and second further injury to the limb The patient should be sent to a hospital immediately by *stretcher* There the legs should be elevated to drain out the edema fluid provided no signs of incipient or actual gangrene are noted The feet should be kept in a cool environment (15 5°–21 1° C 60–70 F) and protected from exposure to heat such as a hot stove or a heated ambulance They should be handled as little a possible and no massage or rubbing should be attempted Local antiseptics and ointments should not be used However strict aseps s must be maintained to avoid infection Protection against pressure necrosis especially in the region of the heel must be observed Measures to prevent secondary infection including administration of tetanus toxo d and penicillin should be carried out

Later Treatment Once the patient is in a hospital the treatment will depend

immersion foot, particularly when hyperesthesia, following return of sensation in injured nerves, is present

SEQUELAE

If credence can be placed in the complaints of patients suffering from trench foot or immersion foot, the various difficulties may persist for as long as 6 or 7 years after exposure However, sometimes the severity of the reported symptoms may be questioned because there is the matter of financial compensation from the government in many instances

The sequelae can be divided into three main categories a classification which is more apparent in trench foot[1] than in immersion foot One group demonstrates

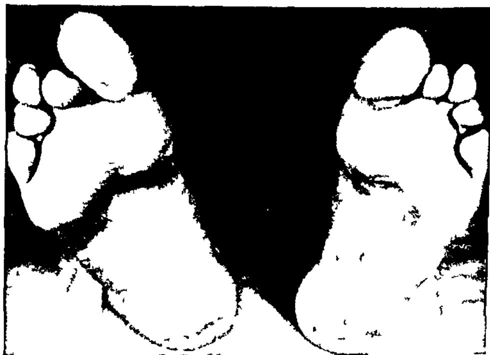


FIG 46 Immersion foot demonstrating atrophy of tissue and rigidity of toes

predominantly findings suggestive of excessive sympathetic activity a low cutaneous temperature cyanosis, hyperhidrosis, a subjective sense of coldness, swelling on prolonged standing and marked responsiveness to extremes of environmental temperature For the most part, the complaints are minimal Generally, aside from the signs already mentioned there is little else that can be noticed on examination The pulsations in the main arteries of the foot are usually present and oscillometric readings are likewise normal

Another group manifests symptoms referable to peripheral nerve involvement The patients in this category complain of numbness, paresthesias burning shooting pains and tenderness particularly over the metatarsophalangeal portion of the foot Objectively one may find areas of hypesthesia to pin prick and light touch these corresponding closely to the sites which are sensitive to deep pressure

The third group, into which most patients fall show signs and symptoms both of excessive sympathetic activity and of peripheral nerve involvement There may also be atrophy of the small muscles of the foot osteoporosis of the small bones,

of disability is likewise lengthened with the degree of impairment depending upon the extent of the nutritional disorder For the most part however, amputation even of toes is rarely necessary

ORDINARY FROSTBITE AND HIGH ALTITUDE FROSTBITE

Ordinary frostbite and high altitude frostbite have many characteristics in common and for this reason they also will be discussed together

Etiologic Factors

Ordinary Frostbite This condition results from protracted exposure to environmental temperatures which are freezing or below Aside from the degree of cold its duration and the wind velocity also determine the severity of frostbite Other contributing factors are individual susceptibility to cold a poor state of nutrition and old age In contrast to trench foot and immersion foot exposure to dampness is not a factor in producing frostbite and in most instances is not present It is of interest that the cases of cold injury arising out of the Korean War are predominantly those of frostbite rather than trench foot This is probably due to the fact that the soldiers and marines for the most part were exposed to much lower environmental temperat [illegible]

co [illegible] differ from common frostbite in several minor respects First the degree of cold is greater (-40 to -52° C -40° to -61.6° F) while the exposure to this agent may only be for a few minutes[3] Second rarely are other parts of the body besides the extremities affected In contrast common frostbite may at the same time involve the flat surface of the face and any other exposed portion

Pathogenesis

The initial effect of exposure to cold in the absence of dampness is a marked and prolonged vasoconstriction of the arterioles leading to a reduced local blood supply This response is accentuated by hunger exhaustion and anxiety Oxygen exchange ceases since dissociation of oxyhemoglobin at a low temperature is negligible If the cold is sufficiently intense the frozen limb solidifies completely When thawing occurs the skin which was previously pale becomes red as a result of capillary dilatation In this hyperemic stage swelling of the involved part appears due to a considerable loss of plasma from the blood stream into the tissue spaces

Pathology

As a result of the concentration of the circulating blood the red blood cells fill the capillaries and form a sludge At first there is no tendency for the cells to adhere to the wall or to organize but after 2 or 3 days real thrombi form The masses of agglutinated red blood cells obstruct the blood stream locally and lead to gangrene of the tissues There are also alterations in the blood vessels themselves

upon the state of the tissues of the foot All desquamating epidermis should be removed by *rubbing lanolin ointment, containing 4% salicylic acid into the skin* The procedure is performed by the patient at frequent and scheduled intervals during the day When desquamation is completed the ointment is replaced by mineral oil and a dilute solution of alcohol for purposes of massage If hyperhidrosis is marked, formaldehyde by ion transfer (Chap XXV) is of value,[1] daily treatment for six days are usually effective in producing temporary alleviation of the condition Gangrenous toes or portions of a foot should not be removed surgically until it is certain that all spontaneous improvement has ceased Frequently the appearance of the necrotic process is misleading since it may only involve the superficial structures Under such circumstances the actual loss of tissue may be much less than first anticipated (Fig 45B D, F, G)

Sympathectomy plays only a limited role in the treatment of the chronic stage of trench foot[14] or immersion foot Although there is little question that it will eliminate such signs of increased sympathetic tonus as coldness of the feet cyanosis, and hyperhidrosis, rarely are these disabling enough to warrant carrying out such a procedure At times sweating is so excessive that maceration of the skin occurs, and under these circumstances sympathectomy is indicated, especially if there is an associated dermatophytosis which is otherwise resistant to treatment This procedure is also of value in accelerating the rate of healing of ulcers, wounds resulting from amputation, and extensive necrotic lesions, provided there is an associated vasospasm

Rehabilitation As soon as the signs of the acute phase of trench foot or immersion foot have disappeared a program of rehabilitation should be instituted If bedridden, the patient should be made ambulatory as quickly as possible preferably without such props as a cane or a crutch He should be taught to walk normally placing his weight on both feet equally In some instances the first attempt is associated with such pain that the patient is fearful of continuing In that case he should attempt to stand and walk correctly while in a pool of lukewarm water, since the buoyancy of the latter helps reduce the load placed upon the feet

Because there is frequently considerable pain in the sole of the foot on assuming the upright position, another heel is attached to the shoe a short distance in front of the ordinary heel in order to remove the pressure from the sensitive portion[1] In this manner the patient is able to walk on both heels with the sole of the shoe off the ground As he continues to be ambulatory he will wear down the anterior heel in the process of which there will be slight at first but gradually increasing pressure applied to the sole of the foot

Prognosis

The prognosis in trench foot will be determined only after repeated examinations of large groups of individuals over a period of many years Even then the question of government compensation will continue to plague the examiner and cast doubt on the significance of the collected data

In immersion foot if paralysis and extensive sensory loss persist into the third week, recovery will generally take many months[1] If gangrene is present the period

consisting of early swelling and vacuolization of the intimal cells and proliferative changes

Clinical Characteristics

Acute Stage Of the various stages into which the clinical course of common frostbite or high altitude frostbite can be divided the first or acute phase corresponds to the period immediately following exposure This generally lasts for several weeks and is characterized by freezing thawing exudation and the production of necrosis[5] Initially the patient will experience numbness of the affected parts at times preceded by a prickling sensation The skin is waxy white and cold but later it becomes red swollen and warm Usually within a day or two of thawing blisters appear (Fig 47) At the beginning these are filled with yellow



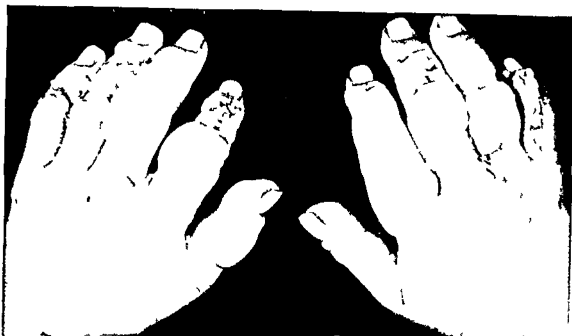


Fig 48 ... esent B Gan ... is J E Scarff ... Surg Gynec ... Dec 1943 [April 1949] The Franklin H Martin Memorial Foundation)

fluid which then becomes hemorrhagic within 3 to 5 days The nail beds are frequently involved in the same process the hemorrhage under the nails giving them a black appearance The distension causes many of them to be shed

Subacute Stage In the next phase resolution of the necrosis occurs associated with the onset of vasospasm and neurologic changes The extent and severity of the gangrenous process can not be determined until late in this stage at which time crusts due to superficial necrosis will generally begin to separate (Figs 48 and 49) The presence of increased sympathetic tonus is manifested by coldness cyanosis excessive sweating and sensitivity to exposure to cold

Neurologic abnormalities are common findings in the subacute stage Sensory loss is generally partial and is stocking glove ... is in the digits The sen... discrimination[5] Deep p... ... are not impaired



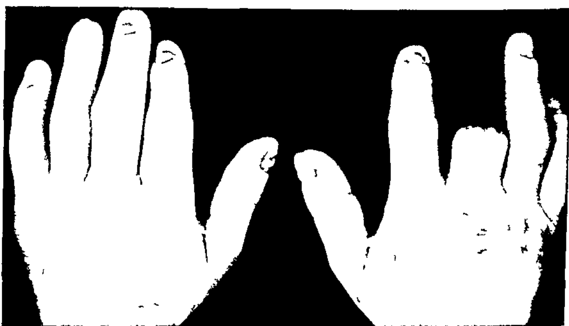


FIG 47 Common frostbite A Large bullae filled with straw colored fluid swelling of hands and necrosis of tissue B After conservative treatment and removal of necrotic tissue on right third finger Note loss of nails

uninterrupted prolongation of the coagulation time (above 30 minutes) is maintained for at least 5 days following exposure[11] Furthermore the anticoagulant should be started within 16 hours after the onset of the condition However it must be pointed out that the above theory has been effectively challenged by a number of other workers[10] It would appear that the routine use of heparin in patients with frostbite should await further trial in the form of large, carefully controlled clinical series

Finally the question of the value of the release of sympathetic tone has not been fully answered In the acute stage of frostbite there appears to be little basis for such a measure and in fact, vasodilatation may be harmful at this time Later when vasoconstriction exists, the use of sympathetic blocking agents may produce alleviation Sympathectomy may be worthwhile in the presence of recurrent ulceration or pronounced vasospasm both of which may contribute to invalidism

Once gangrene has formed it is advisable to wait until a line of demarcation appears and then to resect within the limits of devitalization (Fig 49) The few millimeters of necrotic tissue distal to the line of separation is left in situ Later plastic operations can be performed

It must be emphasized that since frequently there may be extensive loss of superficial tissue with little or no damage to underlying structures, surgical intervention should always be conservative This view is supported by the fact that the ability of deep tissues to return to normal function after frostbite is often excellent Such an approach is in contrast to that observed in chronic occlusive arterial vascular disorders in which gangrene of the superficial tissues generally indicates that a similar process is occurring in the deeper structures

Later Therapy When the patient has recovered sufficiently to be ambulatory the steps utilized are similar to those outlined earlier for trench foot Emphasis is placed on the correct use of the involved limb in performing its normal function An intensive physical therapy program is essential

CHILBLAINS (PERNIO SYNDROME)

Chilblains are a clinical entity resulting from cold injury characterized by blotchy changes in the skin itching erythema and in the later stages chronic ulceration of the skin *The fact that the condition is rarely seen in the United States while being frequently noted in England during the winter months may be attributable to the absence of central heating and of heated public vehicles in the latter country*[9] Clinically chilblains can be divided into the acute stage which is completely reversible and a chronic stage in which permanent tissue alterations may or may not be present[2]

ACUTE CHILBLAINS

Etiologic Factors The main factor in the production of acute chilblains is exposure of a limb to cold and damp followed by *warmth* This sequence of events may result in severe spasm and then injury to the cutaneous vessels producing the characteristic signs and symptoms of a toxic erythema[9] However it is neces

Associated with the above are frequently found changes in the skin and small bones *Cutaneous atrophy and sclerosis* are evident in previous sites of superficial necrosis and also to a lesser extent in other areas The abnormalities in the digits consist of shortening thinning of the digital pulp pad thickening and irregularity of the nails, and loss of normal wrinkling of the skin

Chronic Stage Once the acute and subacute phases of frostbite have passed and whatever necrotic tissue was present has been removed the patient enters the

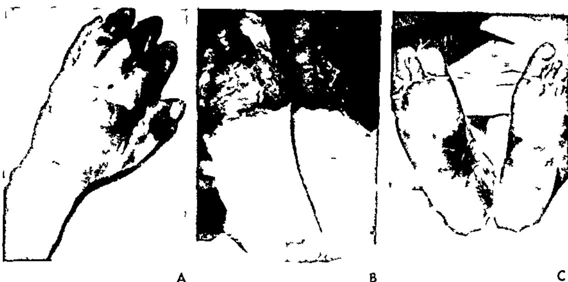


Fig 49 Common frostbite A Gangrene of fingers Wrinkling of skin present B Gangrene of distal portion of both feet C More extensive gangrene of the feet

chronic stage The rigidity of the foot or hand and the changes in the digits become much more marked Vasospasm may begin to recede or may persist for many months Pain becomes a much more frequent and severe complaint being located not only in the areas of scarring following amputation but also in the more proximal portion of the limb Ankylosis of the joints of the digits is a common finding

Treatment

Early Therapy Considerable difference of opinion exists regarding the early treatment of frostbite especially as to whether rapid or slow thawing should be attempted On one point, at least there appears to be agreement—that the involved limb should not be rubbed with snow Most experimental studies[6] and some clinical data suggest that immediate rapid thawing of the frozen part, using a bath temperature around body temperature results in less tissue loss than any other type of procedure Overheating of the limb however, is dangerous The involved portion should be dressed aseptically and either tetanus toxoid booster injection or tetanus antitoxin and penicillin should be given to prevent infection

Another controversial point is the use of heparin According to some workers[8] the early intravenous administration of this drug will prevent the formation of true agglutinative thrombi from the clumped erythrocytes and thus reduce the possibility of necrosis Such a procedure is considered effective only if a continuous

be limited to a minimum and warm clothing should be worn under these circumstances In the case of the female elastic stockings may be desirable in the winter both for warmth and to prevent stagnation of fluid in the tissues Tight and restricting garments the maintenance of one position for long periods, and exposure of cold extremities to concentrated heat are also to be avoided

Active Therapy A number of measures have been proposed in the treatment of acute chilblains Among these are stimulation by electrical and radiation therapy massage and passive and active movements Exposure to ultraviolet light and the oral administration of thyroid extract and nicotinic acid have also been suggested

Prognosis

Despite the use of various types of treatment some patients will not respond Unless such individuals are able to move to a warm and more even climate the disorder may produce a certain amount of disability because of its yearly occurrence and its persistence during cold weather

CHRONIC CHILBLAINS (CHRONIC PERNIO)

Chronic pernio is a vascular disorder characterized by the formation of red hard elevated painful lesions on the exposed surfaces of the extremities which appear during the winter and gradually subside in the late spring and early summer[13] It is present predominantly in females beginning in adolescence or early childhood The condition occurs in susceptible individuals if the limbs are exposed to cold repeatedly and for prolonged periods of time Generally there is progression over several winters to a stage of permanent discoloration nodule formation and finally ulceration of the skin[2]

Pathogenesis The altered physiology consists of spasm of the smaller cutaneous vessels to the point of marked anoxia of the tissues As a result necrosis and ulceration occur followed by changes in the skin which resemble scleroderma The precipitating factor in a susceptible patient is a drop in environmental temperature not necessarily to the point of freezing It is of interest that the skin of a normal individual exposed to the same conditions would not be affected to any appreciable extent Excessive fat in the leg is a predisposing factor probably because this tissue is poorly vascularized[14]

Pathology The histologic alterations are not [illegible] Characteristically they consist of an angiitis o[illegible] and later necrosis of the fat and the appeara[illegible] indicate [illegible] these findings tion [illegible] The vascular reaction inflam[illegible] and perivascular [illegible] are found in the typical case of chronic chilblains

Clinical Characteristics

The early findings in chronic chilblains are blotchy reddish purple discolorations of the limbs appearing in cold weather These color changes fade into the

sary to point out that only certain individuals will react to such a situation by developing the condition. A young person, especially at puberty, is more susceptible than an adult. Chronic ill health and debility and a sedentary existence may be contributing factors.

Clinical Characteristics

Generally with the onset of cold weather, the susceptible individual will begin to experience burning and itching of the extremities on exposure to cold. The symptoms may be followed by swelling and cyanosis or redness of the skin. If the patient remains in the cold for any period of time, blebs of varying size, at times filled with blood, may develop. Upon coming into a warm environment, the itching and burning become intensified. Too rapid warming by placing the limbs *near an open fire or in hot water may produce blistering if not already present*.[1] The acute stage is fully developed within 12 to 24 hours after the initial exposure and lasts only a few days unless the limbs again come in contact with cold. Under the latter circumstances the condition is markedly aggravated.

Although generally noted on the digits, the skin changes may less frequently be present on the ears or nose, the breasts, and the proximal portions of both the upper and lower extremities. They may persist with exacerbations throughout the winter extending even into the summer. A complication is the deposition of calcium salts into the skin in the form of nodules which break down and ulcerate.

Differential Diagnosis

Acute chilblains located on the legs must be differentiated from several entities characterized by the presence of masses or ulceration. Among these is erythema nodosum (Chap. XXI) in which tenderness, pain and fever are associated with the existence of the lesions. On fading, the latter give the characteristic appearance of bruising. Erythema nodosum may follow an acute upper respiratory infection or acute rheumatic fever or it may be a manifestation of tuberculosis. In contrast with acute chilblains, it is not related to exposure to a cold environment.

Erythema induratum (Chap. XXI) is a deep seated lesion which may form a *penetrating ulcer with a sloughing base*. In acute chilblains, on the other hand, the involvement is superficial. Again, exposure to cold does not play a role in erythema induratum.

Erythema multiformi may mimic acute chilblains when the latter condition manifests toxic erythema of the extremities. However, the eruption in erythema multiforme is usually more profuse and of a particular pattern.[9] The attacks generally occur at long intervals, not necessarily in the winter months.

Treatment

Prophylaxis. As in the case of all entities produced by cold injury, the first approach to therapy in acute chilblains is prophylaxis. Since the condition is an expression of an individual susceptibility to cold,[9] exposure to this stimulus should

break down to produce ulceration. At this stage pain is much less severe. With a rise in environmental temperature the ulcer may begin to heal slowly, becoming covered by scar tissue and deep pigmentation. The overlying skin is atrophic and scaly. In the severe long-standing cases complete recovery may not occur even during the summer. It is necessary to point out that not all lesions progress to the stage of ulceration, but instead there may be regression of the process.

Differential Diagnosis

Chronic chilblains have been frequently mistaken for several other conditions, especially erythema induratum (Bazin's disease) and nodular vasculitis. In fact there is some question as to whether all these disorders are not the same entity.[1] Typically in chronic chilblains there are recurrent attacks which appear in the winter and disappear in the summer, but this may also be true in some cases of erythema induratum. However, the ulcers of chronic chilblains are usually more superficial than those of erythema induratum and the degree of inflammatory reaction is not as great. (For further differential diagnosis see Table 8, p. 78, and Ch. p. XXI.)

Treatment

Therapy for chronic chilblains involves, for the most part, proper protection and minimal exposure of the extremities to cold. If at all practicable the patient should move to a warm climate. For the actual lesions the treatment is similar to that outlined for stasis ulcers (Chap. XVI). Since an essential factor in chronic chilblains is arteriolar vasospasm, sympathectomy has been suggested as treatment and in some instances it has prevented recurrence of the lesions.[12] At the same time the procedure appears to relieve the sense of coldness, heaviness and burning. However, the thickness of the ankles, the pigmentation and the color changes are not substantially improved. Histamine desensitization has also been given a clinical trial. The initial dose is 0.05 mg of histamine base injected subcutaneously three times weekly, with a gradual *increase* in quantity over a two-month period to 0.35 mg. Then a maintenance dosage of 0.[illegible] mg three times a week should be given during the entire period of cold weather.[4] The rationale for this therapy is not clear.

Prognosis

If the disease is not recognized early in its inception, the repeated yearly attacks of ulceration and scarring may produce unsightly blemishes, permanent disfigurement of the skin, and repeated and long periods of incapacitation.

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surrounding skin which is generally abnormally cold and redder than normal with prominent hair follicles [1-] The lesions are usually present on the lower third of the legs, particularly the medial malleolus (Fig 50), although at times they extend down to the toes and up to below the knee Occasionally they are noted on the hands At first the discolorations disappear during the summer to recur in the



Fig 50 Typical cutaneous lesions of chronic pernio

winter, but with repeated attacks they persist Eventually they may become larger swollen, and nodular

As the masses form, the patient experiences burning and itching in the involved sites, followed by redness and excruciating pain locally with progression of the process Examination at this stage will reveal firm painful and tender lesions, from a few millimeters to several centimeters in diameter With further elevation of the masses, the overlying skin becomes very thin and assumes a deep red or violaceous color Then a serosanguinous or purulent secretion forms as the lesions

break down to produce ulceration At this stage pain is much less severe With a rise in environmental temperature the ulcer may begin to heal slowly, becoming covered by scar tissue and deep pigmentation The overlying skin is atrophic and scaly In the severe long standing cases complete recovery may not occur even during the summer It is necessary to point out that not all lesions progress to the stage of ulceration but instead there may be regression of the process

Differential Diagnosis

Chronic chilblains have been frequently mistaken for several other conditions especially erythema induratum (Bazin s disease) and nodular vasculitis In fact there is some question as to whether all these disorders are not the same entity [1] Typically in chronic chilblains there are recurrent attacks which appear in the winter and disappear in the summer but this may also be true in some cases of erythema induratum However, the ulcers of chronic chilblains are usually more superficial than those of erythema induratum and the degree of inflammatory re action is not as great (For further differential diagnosis see Table 8, p 78 and Chap XXI)

Treatment

Therapy for chronic chilblains involves for the most part proper protection and minimal exposure of the extremities to cold If at all practicable, the patient should move to a warm climate For the actual lesions the treatment is similar to that outlined for stasis ulcers (Chap XVI) Since an essential factor in chronic chilblains is arteriolar vasospasm sympathectomy has been suggested as treatment and in some instances it has prevented recurrence of the lesions [1-] At the same time the procedure appears to relieve the sense of coldness heaviness and burning However the thickness of the ankles the pigmentation and the color changes are not substantially improved Histamine desensitization has also been given a clinical trial The initial dose is 0.05 mg of histamine base injected subcutaneousl three times weekly with a gradual increa e in quantity over a two month period to 0 35 mg Then a maintenance dosage of 0 2 mg three times a week should be given during the entire period of cold weather [4] The rationale for this therapy is not clear

Prognosis

If the disease is not recognized early in its inception, the repeated yearly attacks of ulceration and scarring may produce unsightly blemishes permanent disfigure ment of the skin and repeated and long periods of incapacitation

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CHAPTER

XX VASCULAR ENTITIES PRODUCED BY TRAUMA OR NOXIOUS AGENTS

(Continued)

4 SYNDROMES RESULTING FROM COMPRESSION OF SUBCLAVIAN VESSELS AND BRACHIAL PLEXUS

In recent years there have been described several syndromes of the upper extremity in which the predominant findings are neurovascular in origin In all of these the initiating factor is intermittent compression of the brachial plexus and/or subclavian vessels in one of three sites behind the scalenus anticus muscle between the clavicle and the first rib or beneath the pectoralis minor muscle

Generally the cause is either some anatomic abnormality or a position of the shoulder girdle and arm assumed by the patient for relatively long periods Although the responsible mechanism is different in each group many of the symptoms and signs are common to all In most instances when compression of the vessels and nerves is removed recovery occurs However repeated and prolonged trauma to these structures may eventually lead to irreversible damage

CERVICAL RIB AND SCALENUS ANTICUS SYNDROMES

Since the manifestations of the cervical rib and the *scalenus anticus* syndromes are for the most part similar these conditions will be discussed together Through usage, the term cervical rib syndrome refers to an entity in which symptoms indicative of trauma to the brachial plexus are found in the presence of a cervical rib When similar clinical findings exist but no osseous anomaly can be demonstrated roentgenologically then the condition is considered a scalenus anticus syndrome The incidence of both disorders is higher among females than among males with most of the patients being 40 to 50 years old

NORMAL ANATOMIC RELATIONSHIPS

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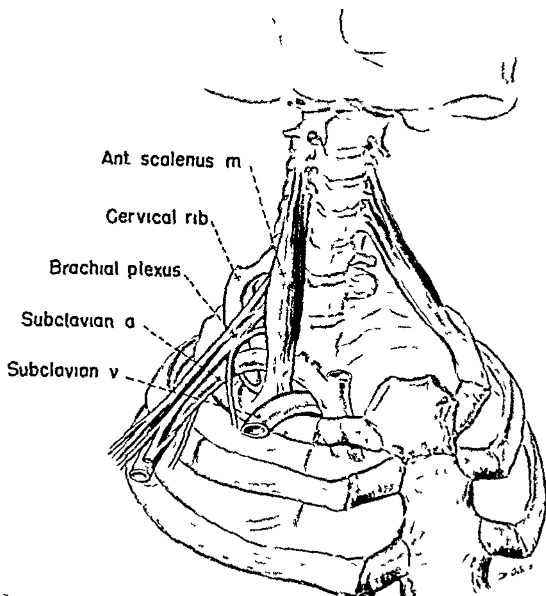


FIG 51 Normal anatomic relationships between the scalenus anticus muscle and the neurovascular structures in the neck

ships that exist between the scalenus anticus muscle and the surrounding tissues and the changes that are produced by the presence of cervical ribs (Figs 51 and 52)

The scalenus anticus muscle arises from the anterior tubercles of the transverse processes of the third to the sixth cervical vertebrae and descends vertically to be inserted into the inner border of the first rib Contraction of this muscle as during respiration causes elevation of the first rib Of significance is the fact that the brachial plexus and subclavian artery pass behind the scalenus anticus muscle to its outer margin and then wind over the first rib

Cervical ribs may take the form of either short osseous structures which just extend beyond the transverse process with or without a free end or almost complete or complete ribs possessing a true cartilage which unites with the cartilage

of the first rib The cervical rib is found in the posterior triangle of the neck which also contains the third part of the subclavian artery the subclavian vein, and brachial plexus

Despite the apparent vulnerability of the neurovascular structures in the neck actually clinical indications of their compression are relatively infrequent Even in the presence of cervical ribs only a small percentage of cases show abnormal findings

Pathogenesis

A number of factors have been proposed as agents in initiating and maintaining a cervical rib or a scalenus anticus syndrome In both conditions the scalenus



Fig 52 X ray showing a formed cervical rib on left side

anticus muscle appears to be mainly implicated with this structure demonstrating either fibrosis spasm or hypertrophy The basis for such changes is not clear *although it may be local trauma or a greater load placed on the accessory muscles* of respiration into which category the scalenus anticus muscle falls In any event as a result of the changes the activity and freedom of movement of the brachial plexus and the subclavian artery are restricted the vessel being compressed slightly with each respiration As the muscle continues to alter in size and consistency the artery is further compressed and displaced backward This pushes the brachial plexus against the floor of the posterior triangle of the neck or if a cervical rib is present against the body of this structure Because of the resulting irritation of those somatic efferent fibers in the brachial plexus which innervate the scalenus anticus muscle the latter structure tends to remain in a state of spasm This response causes increased elevation of the first rib with further trauma to the brachial plexus and perpetuation of spasm of the scalenus anticus muscle

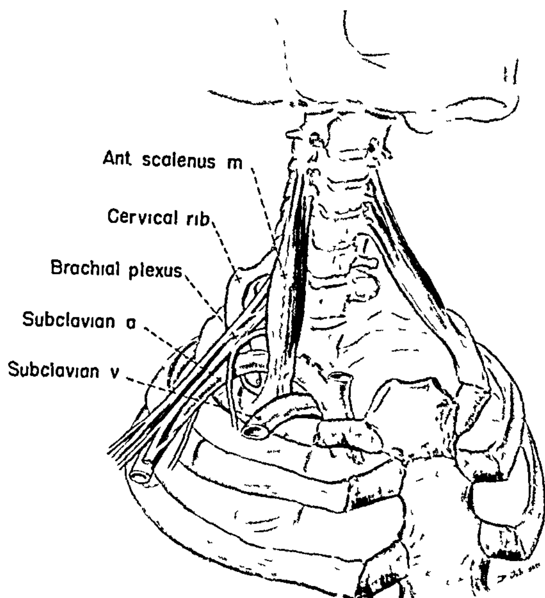


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Cervical ribs may take the form of either short osseous structures which just extend beyond the transverse process with or without a free end, or almost complete or complete ribs, possessing a true cartilage which unites with the cartilage

Hence, one would not expect the vasomotor phenomena to be as conspicuous a feature in this condition.

DIAGNOSIS

There are several tests which are of value in determining whether or not a scalenus anticus or a cervical rib syndrome exists. One consists of an examination of the supraclavicular fossa. The presence of tenderness, tenseness or hypertrophy of the scalenus anticus muscle helps support either diagnosis. The immediate relief of pain in the arm following the injection of procaine into the belly of this muscle is further evidence. Naturally, all patients suffering from pain in the arm should have x-ray studies of the cervical spine. The existence of a cervical rib, in the face of neurologic and vascular findings in the arm, makes the diagnosis of a cervical rib syndrome practically certain. However, in all instances the arm and shoulder should be placed in various positions and the effect on the pulse at the wrist determined.

The Adson maneuver is the most commonly positive test in both scalenus anticus and cervical rib syndromes. The patient, seated with his arms resting on his knees, turns his head to the affected side, hyperextends the neck by elevating the chin, takes a deep breath, and squeezes down with the glottis closed. A positive response is manifested by a reduction or complete absence of the pulse at the wrist. The change can be confirmed by the use of an oscillometer. The cuff is placed around the forearm and the maximal swing of the oscillometer needle is determined. Then while the above maneuver is being carried out, this step is repeated. An absence or reduction in the reading indicates that compression of the subclavian artery has occurred.

TREATMENT

No unanimity exists regarding the proper therapeutic approach in both the scalenus anticus and the cervical rib syndromes. There is little question, however, that all available medical procedures should be exhausted before resorting to surgery.

Medical Approach. In the milder forms of scalenus anticus syndrome, corrective exercises and some type of support to pull the shoulder girdle up and backward may give considerable and prompt relief.[4] When the syndrome is the result of direct or indirect trauma to the scalenus anticus muscle, rest to the part with the arm in an elevated position will also alleviate the symptoms.

Repeated procaine injections into the muscle belly are worthwhile therapy. The procedure is performed as follows:[8] The patient's head is brought over to the painful side to relax the sternocleidomastoid muscle. The latter structure is then pushed medially just above the clavicle and at the same time the examiner's fingers are forced inward and downward and the patient's head is pressed to the opposite side and retracted. The scalenus anticus muscle now becomes palpable so that it can be straddled with two fingers, which are then pushed down firmly, causing the muscle to bulge between them. A 0.9 cm (3/8 inch) hypodermic needle is inserted between the fingers into the muscle belly, and 2 cc of 2%

In the case of the cervical rib syndrome, *there are some workers who believe* that the rib itself also plays a role in producing compression of the neurovascular structures. Even if it is small, at times it possesses a firm fibrous cord which extends from the tip to the first thoracic rib; this structure may serve as a ridge across which the lower trunk of the brachial plexus can be traumatized. Furthermore, the subclavian artery *may be compressed by the cervical rib at the lateral* border of the scalenus anticus muscle or between the anterior end of the rib and the clavicle.

Clinical Characteristics

Symptoms. The clinical picture in both *cervical rib and scalenus* anticus syndromes depends to a great extent upon the structures compressed and the degree of permanent change that ensues. The most common symptom is pain in the limb which may be a dull ache or sharp and lancinating. It is generally due to pressure on the brachial plexus and follows the course of the ulnar and median nerves into the upper extremity. It may be unilateral or bilateral and is also present in the shoulder and, at times, in the neck. The symptom is constant in type and is initiated by some sudden or violent exertion. Once present, it is exaggerated by rotation of the head or a forceful downward pull of the shoulder. Associated with the pain in the arm are frequently found paresthesias and formication in the fingers.

Physical Findings. Pressure on the brachial nerves also produces certain signs, among which are hypesthesia and anesthesia in the involved hand and digits. Late *in the course of the disease a mild atrophy or wasting of the muscles supplied by* the brachial plexus may also be observed. This is particularly prominent in the thenar and hypothenar eminences and in the interosseous muscles. The strength of the grip may be diminished.

The frequent findings of vascular abnormalities are due either to transient or permanent changes *in the lumen of the subclavian artery* or vein or to pressure on the sympathetic fibers in the brachial plexus.[11] Periodic compression of the subclavian artery may result in temporary impairment of muscle blood flow, this manifesting itself as an inability of the patient to work with his hands raised above his shoulders, to drive a car, or to lift heavy objects. Permanent structural changes are associated with more marked clinical signs. If complete occlusion of the subclavian artery occurs, pulsations in the brachial, radial, and ulnar arteries will be lost. Such a change, if it takes place more rapidly than collateral vessels develop, *may cause nutritional disturbances in the fingers, on occasion even to the* point of gangrene.

If irritation of the sympathetic nerves in the brachial plexus results, the vascular changes may take the form of increased sympathetic tonus. This may manifest itself as a decrease in cutaneous temperature of the involved hand, as compared with its mate, hyperhidrosis, puffiness of the hand, and a duskiness to the skin. A history of Raynaud's phenomenon may be elicited in some patients. On occasion actual destruction of the sympathetic fibers will occur, with the production of a Horner's syndrome (p. 445). *In the scalenus anticus syndrome the cervical sympathetic fibers are less likely to be irritated than in the cervical rib syndrome*

to those observed in the cervical rib and scalenus anticus syndromes paresthesia or anesthesia muscle weakness in the hand and trophic disturbances (muscle atrophy and deformities of the nails) Among the vascular findings are color change in the hands and swelling

DIAGNOSIS

In order to make the diagnosis of costoclavicular syndrome the shoulder attention posture must initiate symptoms and produce a definite reduction or loss of arterial pulsations Assumption of a relaxed position of the shoulders should result in disappearance of complaints and a return of normal pulsations The diagnosis is further strengthened if the patient relates a history of having maintained the precipitating position for considerable periods of time A differential point between this condition and the scalenus anticus syndrome is the finding that anesthetization of the scalenus anticus muscle with procaine does not affect the symptoms (see above)

TREATMENT

Postural exercises may correct mild cases by strengthening the levator scapulae and trapezius muscles The patient should be instructed not to throw his shoulders back but to allow them to hang freely or even to drop slightly forward In the severe cases a segment of the compressing rib may be removed

HYPERABDUCTION SYNDROME

The hyperabduction syndrome[1] is an entity in which numbness and paresthesias in the hands and occasionally even gangrene of the fingertips are associated with repeated obliteration of the pulses at the wrist as a result of prolonged periods in which the arms are maintained in hyperabduction above the head Since the latter maneuver causes the disappearance of the pulse in the great percentage of normal persons this response has pathologic significance only if it is associated with findings that suggest pressure on the brachial plexus and subclavian artery and vein Furthermore a history must be obtained that the patient assumes the precipitating position for relatively long periods of time as during sleep or in the course of his occupation Finally there should be a marked reduction in symptoms and signs when the position of hyperabduction is abandoned

PATHOGENESIS

The mechanism responsible for the hyperabduction syndrome consists of pressure on the vessels and nerves at two sites[1] One is the point at which the trunks of the brachial plexus pass posterior to the pectoralis minor just beneath the coracoid process With the arm along the side the subclavian artery and vein and the nerves to the arm are relaxed and protected but when the extremity is hyperabducted these structures are stretched around and beneath the coracoid process at the same time that the pectoralis minor is drawn tight As a result the vessels and nerves are subjected to stretching pinching or torsion The second

procaine solution is injected Complete relief of pain should occur within one minute after the anesthetic enters the tissues

Surgical Approach When conservative measures fail, traction on the cervical spine or division of the scalenus anticus muscle may have to be performed[4] Traction is obtained by means of steel hooks inserted subperiosteally beneath the zygomae 2 3-4 6 Kg (5-10 lb) of weight are utilized Although symptoms may disappear within 6 to 8 hours the procedure should be maintained for 10 days The patient must wear a light cervical collar for two weeks Heavy lifting should be avoided for at least the following month

Scalenotomy is another surgical procedure for scalenus anticus syndrome with resection of the distal portion of the muscle if it is found to be markedly hypertrophied It has been suggested[6] that if a preoperative stellate ganglion block produces a reduction in pain, a thoracic sympathectomy performed in conjunction with scalenotomy, may increase the chances of success Such a measure deserves further investigation, since with scalenotomy alone relief can not be expected in more than one third of the cases[1, 6] Perhaps more careful selection of patients for operation may also reduce the number of failures

The surgical treatment of cervical rib syndrome is likewise scalenotomy and sectioning of the insertion of the scalenus anticus muscle When the cervical rib is completely formed and is situated high in the neck, resection of this structure should also be carried out Otherwise it is left intact One can expect better results with scalenotomy in the cervical rib syndrome than in the case of the scalenus anticus syndrome relief of symptoms with this procedure has been reported in one half of the former cases and definite improvement, in about one third[1]

In the course of the operation any other structures encountered which might conceivably exert pressure on the vessels or the brachial plexus should be divided A fairly frequent finding is a strong fibrous band running from the tip of the transverse process of the seventh cervical vertebra to the first rib and simulating a cervical rib Another is a distinct thickening of Sibson s fascia which also passes from the transverse process of the seventh cervical vertebra to the first rib[7]

COSTOCLAVICULAR SYNDROME

The costoclavicular syndrome *is another condition in which* vascular and neuritic complaints are produced in the upper extremities through intermittent compression of the subclavian artery and/or the brachial plexus The responsible mechanism *is a narrowing of the space between the clavicle and the first* thoracic rib brought about by holding the shoulders downward and backward as when a soldier carries a heavy pack on his shoulders or when he stands at attention

Clinical Characteristics

Commonly noted in the costoclavicular syndrome are neurologic symptoms consisting of lancinating pain in the scapular region that radiates up the back of the neck and down the arm[9] It may be aggravated by depression of the shoulders or pressure lateral to the scalenus anticus muscle The physical findings are similar

SCAPULOCOSTAL SYNDROME

The scapulocostal syndrome is a condition which is characterized by pain and discomfort in the shoulder girdle It is caused by long standing change in the relationship between the scapula and the posterior thoracic wall [10] The resulting postural strain probably produces a faciitis or fibrositis which is responsible for the symptoms

The syndrome can be divided into three groups The primary type occurs in middle aged persons and is due to round shoulders and drooping of the shoulder girdle on standing or sitting [10] Improper bed posture produced by the use of high pillows that permits the shoulders to sag and the head to be drawn to one side, is another etiologic factor [10] The secondary type may be found as a late complication of such conditions as subdeltoid bursitis dislocation of the shoulder, and prolonged immobilization of the arm following fracture Patients who have recently become ambulatory after a long period of bed rest may likewise suffer from this syndrome The last group is the static type observed in individuals who are severely disabled due to hemiplegia an amputation or a shortening of one limb from whatever cause

Clinical Characteristics

The most common complaint is pain deep in the shoulder region Often it radiates either to the occiput or spinous processes of the third and fourth cervical vertebrae or down the arm and into the hand along the distribution of the ulnar nerve At times the symptom may be limited to the forearm and hand without any associated complaints in the shoulder or arm

Diagnosis

An important diagnostic sign is a definite trigger point beneath the upper medial angle of the scapula in proximity to the posterior chest wall To elicit the finding it may be necessary first to have the patient place the involved hand on the opposite shoulder with the arm held horizontally to expose the subscapular area The examiner standing behind the patient on the normal side draws the elbow across the chest to increase the adduction of the arm while exerting pressure on the superior medial angle of the scapula In the presence of the scapulocostal syndrome extreme local tenderness and radiation of pain in the affected areas are produced by the digital pressure

A modification of the test consists of having the examiner hold the wrist of the involved limb so that the arm is extended and internally rotated as far as possible Digital pressure is then applied to the same site on the back a positive response again being local pain and radiation

There is usually some difference in the findings in the various clinical types For example limitation of the range of movement of the glenohumeral joint is only minimal in the primary form and much more marked in the secondary Trigger points are much more difficult to locate in the latter since there is generally

point of pressure is the site where the neurovascular structures pass between the clavicle and the first rib Hyperabduction of the arm appears to reduce the size of the space and to allow for compression of the vessels or nerves

Clinical Characteristics

The symptoms and physical findings in the hyperabduction syndrome can be explained on the basis of pressure on the vascular or nervous structures, or on both If no changes in pulsations are noted one can attribute the paresthesias, pain, and numbness of the fingers directly to stretching and pinching of the nervous elements, as well as to ischemia of the nerves from occlusion of their nutrient vessels by the same maneuver If the pulse is occluded, the symptoms are probably also due to anoxia of all tissues, including the nerves as a result of cessation of arterial circulation Why a great number of persons can obliterate their pulses by hyperabduction and still not suffer from the symptoms noted in this syndrome can be explained by the fact that in most instances the periods of ischemia are only temporary When pathologic changes do occur these result from prolonged occlusion of the vessels and permanent damage to the nerve trunks

Diagnosis

When pain paresthesias numbness and swelling of the hands are present it is essential to determine whether or not the pulses can be obliterated in the hyper abduction position To accomplish this, the patient should be seated with the examiner standing behind him and after the pulse at the wrist is checked with the arms along his sides each limb should be moved passively through a 180 degree semicircle During this maneuver the examiner s fingers are kept on the radial artery at the wrist and note is made of the position if any, in which there is a reduction or disappearance of pulsations If a change occurs the response is checked with the patient in the supine position using the oscillometer instead of palpation of the pulse

Treatment

Therapy in the hyperabduction syndrome consists primarily of the avoidance of the precipitating position in sleep and at work At night this may be difficult to achieve since in some patients sleeping with their arms over their heads is a firmly entrenched habit A position of relative adduction can be maintained by tying gauze loosely around the wrists and fastening it to the foot of the bed so that the patient can move the wrists up to approximately the level of the heart but no further[3] This permits considerable freedom of motion but still prevents sleeping with the hands over the head Even with such a procedure, it may take weeks before the habit can be broken Sedatives may be necessary in the interval The patient should avoid excessive strain or injury to the arms and shoulder girdle and should indulge in no procedure which requires hyperabduction of the arms

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tenderness over a wide area At the same time the scapula can not be retracted[10] In the static type little change in symptoms occurs with passive movements

TREATMENT

Treatment consists of postural exercises to correct the stoop The patient should stand or sit with shoulders drawn backward and spine erect and avoid slouched positions To produce a firm support during sleep, fracture boards are placed beneath the mattress and the fewest possible pillows are used A well fitting lumbosacral support will frequently control the lumbar lordosis and thus correct the sagging of the shoulders

Local anesthetics are useful in treating the trigger points, in an effort to break the reflex arc responsible for the pain Repeated blocks with 5–10 cc of 1% procaine or 2–5 cc of 2% Intracaine* in oil have been found efficacious With the latter drug, the anesthetic effect may be active for weeks at a time[10] Either solution is injected into the subscapular tissues after the subscapular area is exposed (see above) Local heat and massage may be of value in conjunction with this therapy

* *β Diethylaminoethyl p ethoxybenzoate hydrochloride*

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CHAPTER

XXI RARE VASCULAR DISORDERS AFFECTING THE EXTREMITIES

This chapter deals with a number of interesting and unusual clinical entities which however are only briefly presented below, since they are rarely observed in general practice A tabular presentation of these entities will be found at the end of the chapter

ACROCYANOSIS

Acrocyanosis is a functional or vasospastic condition in which there *is a* persistent uniform cyanotic rubor to the skin of the hands and feet (Fig 2B p 28) associated with a reduced skin temperature This type of *response is present both* in warm and cold environments although more marked in the latter

Pathogenesis The underlying mechanism is not clear However *there is some* evidence to indicate that the essential physiopathologic *characteristic is* persistent arteriolar spasm at ordinary environmental temperatures *which is associated* with capillary and venous dilatation *Whether the* vasomotor *system is* responsible for the arteriolar spasm or whether *the fault is* entirely an intrinsic change in tone of the small vessels of the skin can not be *decided on the* basis of the present information In any event *due to* capillary *stasis* the quantity of reduced hemoglobin in the blood entering the subpapillary venous plexus is increased causing the cyanotic hue to the skin

Clinical Characteristics The skin color *may* vary from a deep purple when the limb is exposed [illegible] n environment [illegible] be part of the [illegible] contrast to Raynaud's *disease* emotional excitation does not play any role as an etiologic *factor nor are there* any episodes of blanching Furthermore the color change *is not limited to the* digits but includes the entire hand or foot as well as adjoining *parts of the* extremities No involvement of the large arteries exists

Hence when cyanosis is observed *in the* presence of a permanently impaired peripheral circulation it must be *considered as a* reflection of an organically slowed cutaneous blood flow rather *than a* primary acrocyanosis Moreover to make the latter diagnosis it is necessary to rule *out such* systemic conditions as

cyanotic congenital heart disease and any pulmonary pathology which interferes with oxygenation of the blood in its passage through the lungs (For further differential points see Table 12, p 116)

Treatment This involves, primarily, avoidance of cold Exposure to a continued warm environment appears to lessen the intensity of the color change On the basis that the alterations are due to arteriolar spasm the use of sympathetic blocking agents, like Priscoline or Hydergine, might be worthy of a clinical trial

Prognosis Acrocyanosis may be regarded as a relatively benign functional disorder devoid of serious consequences Still, at times it may cause a certain amount of discomfort and disability, particularly if swelling and stiffness of the fingers are prominent findings

LIVEDO RETICULARIS

Livedo reticularis is another rare functional or vasospastic disorder, in which cyanosis takes the form of a mottled, blotchy pattern (Fig 2E p 28) affecting the skin of the lower extremities and, to a lesser degree, of the upper extremities The reticular bluish discoloration produces a meshwork which outlines normal appearing skin The etiology of livedo reticularis is not known

Pathogenesis and Pathology The characteristic abnormality is a marked vasospasm of the arterioles of the skin, producing atonic dilatation of the capillaries and venules and stasis of local circulation Because of the impaired cutaneous blood flow skin temperature may remain subnormal for prolonged periods even when the limb is exposed to a normal environmental temperature Pathologic studies[1] have revealed that there may also be some organic changes in the arterioles of the skin such as proliferation of the intima and perivascular infiltration

Clinical Characteristics Aside from the esthetic effect of the mottling livedo reticularis is generally not associated with any symptoms At times, however, a sensation of coldness, numbness paresthesias of the feet and legs or dull aching may be experienced Physical examination reveals no signs of involvement of the main peripheral arteries and all tests for arterial and venous efficiency are normal On occasion there may be recurrent ulceration of the skin of the legs and very rarely gangrene of the toes

It is possible to divide livedo reticularis into three clinical types[8] In one cutis marmorata, the mottling is initiated by exposure to cold and soon disappears in a warm environment This change is noted rather commonly in infants and is not associated with any other disorder In the second group livedo reticularis idiopathica, the color manifestations are more marked and are not reduced by exposure to a high environmental temperature In the third category livedo reticularis symptomatica the mottling is also persistent but there are associated signs of involvement of the cutaneous and subcutaneous vessels by some other pathologic process, such as erythema induratum or syphilis

Treatment As in the case of acrocyanosis most patients with livedo reticularis require no treatment other than reduction of exposure to cold to a minimum In

those rare instances in which ulcerative areas form on the legs sympathectomy may help initiate healing Although in general the course is benign the patient may seek medical treatment because of the blotchy skin

ERYTHROMELALGIA

Erythromelalgia is a vascular disorder which is characterized by episodes of increased cutaneous temperature rubor of the skin and a bilateral sensation of severe burning in the extremities precipitated by a rise in the immediate environmental temperature The latter may result from covering the feet with socks and shoes or with bed clothes at night or from exposing the limbs to a warm room or to the heat of the summer months

Pathogenesis The altered physiology responsible for the symptom complex is not clear All evidence points to a definite increase in peripheral blood flow through both the large superficial and deep arteries of the limb the augmented circulation in the cutaneous vessels producing the rubor of the skin and the increased skin temperature The same factor may also be responsible for the characteristic burning sensation the vascular tension producing pressure on and irritation of adjoining nerve endings However this does not seem to be the full explanation since an equal increase in peripheral blood flow in a normal extremity will not induce such a symptom

Studies of capillary blood flow have revealed an exaggerated reaction of the *minute vessels* to warmth in the form of marked dilatation and a significant rise *in capillary pressure*[8] This type of response has been explained on the basis of an absence of normal antagonistic vasoconstriction

It is the opinion of other *workers*[4] however that erythromelalgia is not a disease entity but rather a symptom *complex seen in* many disorders and not necessarily associated with vasodilator *phenomena* According to this view a variety of noxious agents *such as chronic* inflammatory conditions of the skin, injury by ultraviolet *rays and freezing* burning and scratching will produce a toneless state of the minute vessels *of the skin* Under such circumstances, exposure of the involved areas to increased *environmental* temperature, extreme cold or local friction as occurs with walking *will* elicit the erythromelalgic type of response However for clinical *application, there* appears to be sufficient basis for considering primary erythromelalgia as a definite disease entity

Differential Diagnosis In most instances the diagnosis of erythromelalgia offers no real difficulty Of prime importance *is the* history of initiation of the *signs* and symptoms either by exposure of the limb to a high environmental temperature or by exercise It is also *of interest that* during an attack *dependency will* exaggerate the complaints while elevation rest, or the local application of cold will reduce them Most *patients with* erythromelalgia have a critical level *of* temperature above which symptoms are *present and* below which they are absent

In order to confirm the diagnosis it may therefore be *necessary* to attempt to elicit an attack of pain by raising the cutaneous temperature beyond the

critical point This can be accomplished either by using a heating cradle over the abdomen, to produce indirect vasodilatation, or by wrapping the feet in blankets

To be considered a case of primary erythromelalgia, there should be no other condition present which could conceivably be responsible for a severe burning sensation in the extremities (see below) Furthermore, all tests of circulatory efficiency should be normal In fact, the amplitude of the peripheral pulses and the oscillometric readings are frequently found to be in the upper limits of normal

Primary erythromelalgia must be differentiated from a number of conditions which demonstrate as part of their clinical picture, red painful extremities (secondary erythromelalgia) Among these are polycythemia vera, thromboangiitis obliterans (Fig 2D, p 28), low grade forms of cellulitis and peripheral neuritis associated with diabetes pernicious anemia and pantothenic acid deficiency An important differential point is the finding that the foot suffering from an occlusive arterial vascular disorder or peripheral neuritis is generally cold not hot

Another symptom complex which may mimic primary erythromelalgia is acroparesthesia This is a subjective sensory disturbance affecting both the upper and lower extremities and characterized by tingling, numbness, burning paresthesia, or formication Women over the age of 30 years are especially predisposed to involvement of the fingertips In such a group there may be an associated disorder of the ovaries Diseases of the spinal cord such as tabes, subacute combined degeneration multiple sclerosis and syringomyelia, have also been found in acroparesthetic patients The burning sensation in the hands and feet is primarily experienced during the night and frequently may interfere with sleep Relief may be obtained by exposing the limb to cold or exercising it It is of interest however that physical effort during the day appears to bring out the discomfort at night In contrast with primary erythromelalgia there are no objective findings during an attack except slight pallor Furthermore, there is no critical environmental temperature which elicits the symptoms

Treatment A great number of therapies have been suggested to prevent or control the attacks of burning pain in erythromelalgia but none has proved very satisfactory The most important measure is the elimination of the precipitating factor—a rise in skin temperature The patient should wear perforated shoes or sandals to allow movement of air in contact with the feet and he should sleep with his feet uncovered If practicable he should move to a climate where the temperature does not reach the critical level at which the episodes of pain are initiated Exposure of the feet to warmth, as while riding in the front seat of an automobile near the heat of the engine is to be avoided

An attempt should be made to decrease the sensitivity of the vessels to heat The involved limbs are first immersed in water at a temperature low enough to elicit no complaints and then exposed to gradually increasing temperatures until real discomfort is produced At this point the temperature of the water bath is reduced somewhat and cautiously raised again in the following daily immersions The steps should be repeated until the patient is able to maintain his extremities comfortably in water at a temperature which previously would have produced the burning sensation

In some patients various medications or measures may be temporarily helpful in reducing the severity of the attacks Among these are aspirin intravenous calcium gluconate small doses of ergotamine tartrate in combination with bella donna and the inhalation of 1 1000 solution of epinephrine[9] The explanation for the relief experienced by the use of such substances as aspirin and calcium gluconate is not clear There is somewhat more rationale for the administration of ergotamine tartrate and epinephrine, since these drugs cause constriction of cutaneous vessels and hence tend to counteract the existing vasodilatation Wrapping the involved limbs in cold wet cloths or immersing them in ice water will have a similar effect

More heroic measures may have to be used if the condition is unresponsive to the above therapies and is severe enough to be disabling Among these are section or crushing of—or injection of alcohol into—the posterior tibial peroneal and sural nerves Anesthetization of the skin of the foot occurs which will last for from 3 to 6 months

Prognosis Primary erythromelalgia although producing considerable discom fort and even disability is never associated with any untoward complications that may result in loss of life or limb—a point which must be emphasized A mis conception exists that this condition is a serious one probably because secondary erythromelalgia found in conjunction with occlusive arterial vascular disorders or polycythemia has frequently been mistaken for the primary type

DERMATOMYOSITIS

Dermatomyositis is a rare disease of the collagen system characterized by a nonsuppurative inflammation and degeneration of the voluntary muscles of the body generally associated with changes in the overlying skin Little is known concerning the etiology of the disorder It affects both children and adults

Pathology The pathologic alterations may be divided into several stages First there is inflammation within the muscle bundles with proliferation of nuclei loss of transverse striations and separation of myofibrils A diffuse round cell infiltration occurs around capillaries arterioles and small sized arteries as well as in cutaneous subcutaneous and muscle tissue Later there is fragmentation of muscle fibers with phagocytosis by large histiocytes In long standing cases muscle destruction is severe and widespread Collections of histiocytes lymph ocytes plasma cells and fibroblasts can be observed in the affected sites Although the blood vessels may be dilated and engorged no signs of endothelial proliferation or other changes in vascular tissues are noted The microscopic findings in the skin are nonspecific and in the chronic stage may closely resemble those of the acute type of scleroderma

Clinical Characteristics The early stage of the disease is typified by mild systemic responses The initial complaints consist of malaise weakness fever weight loss and vomiting which last for about 3 weeks and are then followed by edema of the affected muscles muscular weakness and tenderness and dermatitis An associated Raynaud s syndrome is common There may likewise

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be *symptoms referable to the joints* which are actually due to involvement of soft tissues or tendons rather than bone

Examination will invariably elicit tenderness of varying degrees over the large muscles of the extremities and elsewhere These structures may at first feel either soft and doughy or, infrequently, firm Later, they become atrophied and less tender At this stage there is restriction of movement due to loss of muscle substance

The abnormal findings may be limited to a group of muscles, such as those of the shoulder girdle or all of the *voluntary muscles may be affected, the latter* response generally occurring in the fulminating type of the disease In the milder cases the involvement is usually bilateral Not only are the changes observed in



FIG 53 Cutaneous lesions seen in dermatomyositis

the extremities and trunk but the frequent findings of dysphagia diplopia and weakness of the tongue and sphincters indicate the extensiveness of the process

The cutaneous changes are not characteristic since they vary so much in degree type and extent of involvement (Fig 53) and at times they may even be *entirely lacking There is no correlation* between the severity of the condition in the skin and that in the muscles At first the cutaneous lesions are those of erythema and edema The swelling is present particularly around the eyes to produce *the heliotrope eyelids of dermatomyositis This finding is* of diagnostic importance, being an early sign and frequently the only cutaneous manifestation [3] As a rule the lids especially the upper ones are swollen and colored a rose pink due to the presence of numerous *closely set telangiectases In the later stages* the eyelids may be sites of a dense or a reticulated form of pigmentation The skin elsewhere may be hard with the changes resembling those of scleroderma A common finding is an eruption over the small joints of *the hands, which early*

in the disease takes the form of ill-defined somewhat edematous blotchy red telangiectatic patches[5] Generally the involvement is bilateral and often symmetrical

Calcino is may also be found in dermatomyositis being present in the subcutaneous tissues and less commonly in the muscles Generally the calcific deposits are noted around such joints as the elbow hip and knee and as in scleroderma the particles of calcium may be expelled through small ulcers located in these regions

Aside from muscle tenderness and atrophy and cutaneous changes the extremities may manifest other abnormalities Pulsations in main arteries may be absent, and reduced oscillometric readings may be obtained These changes may be associated with ulcers on the tips of the fingers which are generally refractory to treatment

Diagnosis Dermatomyositis can mimic disseminated lupus erythematosus scleroderma and scleredema since fundamental disturbances of connective tissue are involved in all four syndromes In most instances a biopsy through involved skin and muscle is necessary to make the diagnosis the most common site for study being the gastrocnemius and pectoralis major An examination of the blood may reveal a mild anemia and an increased sedimentation rate Although the A/G ratio is generally normal mild albuminuria is a rather constant finding Urinary creatine is usually increased in the early course of the fulminating form of the disease and within normal range in the localized chronic type

Treatment Since the etiology of the disease is unknown symptomatic measures are indicated These consist of concentrates of vitamins to support the diet and as much active movement as possible to prevent fixation of joints and formation of contractures A course of Neostigmine given intramuscularly in dosages of 1 cc of 1 2000 solution daily may produce a beneficial result on occasion Testosterone has also been suggested because of its nitrogen retaining power Recently ACTH and cortisone have been used in dermatomyositis with apparently encouraging results However all that can be hoped for from a clinical trial with these medications is a long remission

Prognosis The course of the disorder varies and may result in either mild incapacitation or death Remissions and relapses are frequent About half those patients who have the myositis limited to a small group of muscles may show recovery the only residuals being some restriction in their activities On the other hand the generalized form of the disease in which most of the musculature is involved results in a progressive downhill course until death occurs in from 6 to 12 months This is ordinarily caused by involvement of respiratory muscles resulting in pneumonia respiratory paralysis or cardiac failure

ERYTHEMA NODOSUM

Erythema nodosum is a symptom complex characterized by the transient appearance of cutaneous and subcutaneous nodules resembling bruises accompanied by fever malaise and migratory arthritis There appears to be no single

cause for the entity Among the more frequent etiologic agents are a variety of infections, such as acute rheumatic fever, syphilis, tuberculosis, upper respiratory infections (especially hemolytic streptococcic involvement of the throat), diphtheria, measles, leprosy malaria, typhus fever, and Boeck s sarcoid In sensitive individuals, the ingestion of certain drugs, like the sulfonamide compounds, iodides and bromides, may also be responsible for the initiation of the lesions The condition predominates in females

Pathology Histologic examination of a nodule reveals infiltration of lymphocytes and polymorphonuclear leukocytes about the vascular network in the middle and lower portions of the corium The walls of the vessels are edematous and capillary dilatation is common There may also be an acute infiltration, with atrophy and necrosis of the fat in the subcutaneous tissue

Clinical Characteristics The typical lesion is a relatively superficial firm tender or painful subcutaneous nodule, 1–2 cm in diameter With the onset of edema and erythema the bruised appearance of the skin occurs At times this type of response is accompanied by ecchymosis into the nodules and elsewhere in the skin Lesions last for from a few days to six weeks and may stop at different stages of development and then regress in the time it took for their formation As involution occurs the color of the nodules may change to greenish gray or brown On occasion they may coalesce and seem to fluctuate, but they do not suppurate or break down to form an abscess or ulcer There is a tendency for attacks to appear in the spring and autumn although rarely are recurrences noted The nodules are usually located on the anterior surface of the legs, sites readily vulnerable to trauma However lesions may also form elsewhere as on the soles of the feet the calves the thighs and the upper part of the arms The sites are in no way related to the location of the superficial veins (For differentiation, see Table 8 p 78)

Arthritis of the ankles knees wrists fingers elbows, and other joints is a common occurrence Pain swelling and on occasion redness and fluid are present The joint involvement is associated with fever between 37 1° and 38 2° C (99° and 101° F)

Treatment There is no specific therapy since the condition is self limited However the use of local wet heat rest and salicylates may give some symptomatic relief There is always the necessity to investigate and control the underlying systemic disorder

ERYTHEMA INDURATUM (BAZIN S DISEASE) AND NODULAR VASCULITIS

Erythema induratum is a chronic disorder characterized by nodules and ulcerations in the lower extremities Although the condition at one time was considered to be due solely to tuberculosis in recent years a nontuberculous type has also been described (nodular vasculitis) The disease occurs most often in girls during adolescence and less frequently in boys and men

Pathology The histologic findings consist of varying degrees of periarteritis,

panarteritis and phlebitis affecting the minute and larger vessels in the subcutaneous tissue In the tuberculous type, typical tubercles with caseation in the center of the lesion may be noted There may also be marked necrosis of fat or extensive fibrosis In the presence of the last two responses vascular changes generally predominate while tubercle formation becomes of minor importance In the nontuberculous type tubercles are absent although there may be foreign body giant cells Areas of necrosis are generally smaller than in tuberculous erythema induratum and at times may even be absent

Clinical Characteristics The clinical findings consist of circumscribed red or bluish red deep seated nodules in the skin and subcutaneous tissues of the leg particularly of the calves which tend to persist for years and commonly break



FIG 54 Ainhum A Typical ring like constriction of fifth toe B X ray in the same case showing corresponding bony changes (Reproduced through the courtesy of A M Vaughn J W Howser and G Shropshear Ainhum (dactylolysis spontanea) Report of two cases from Illinois Ann Surg 1_ 868 1945)

down The ulcerative lesion generally becomes painful and tender It is usually irregularly shaped with a ragged undermined edge and a granulating base secreting a watery discharge Healing is slow and is frequently delayed by new crops of nodules Eventually atrophic depressed scars form at times surrounded by pigmentation With repeated attacks an associated edema of the legs and feet may develop probably due to lymphatic obstruction consequent to the inflammatory process

Differential Diagnosis In tuberculous erythema induratum there are usually signs of the underlying disorder elsewhere in the body The intracutaneous tuberculin test is also generally positive In the nontuberculous type it may be necessary to resort to biopsy of a nodule in order to make the diagnosis There should be no difficulty in differentiating erythema induratum from superficial throm

cause for the entity Among the more frequent etiologic agents are a variety of infections, such as acute rheumatic fever, syphilis, tuberculosis, upper respiratory infections (especially hemolytic streptococcic involvement of the throat), diphtheria, measles, leprosy, malaria, typhus fever and Boeck's sarcoid In sensitive individuals, the ingestion of certain drugs, like the sulfonamide compounds iodides, and bromides, may also be responsible for the initiation of the lesions The condition predominates in females

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Pathology The histologic findings consist of varying degrees of periarteritis

Table 17 *(continued)*

Clinical entity	*Sex or race difference*	*Pathogenesis or pathology*	*Characteristic points in history*	*Symptoms pr sent locally*	*Characteristics of lesion or change in skin*	*Signs of arterial or venous impairment*	*Findings elsewhere in body or systemic reactions*
Erythema nodosum	None	Edema of wall of cutaneous ves sels perivas cular infiltration	History of recur rent a d tran sient attacks of lesions in form of crops	No pain some tenderness	Nodules resembling bruises on tibial and ulnar surfaces of limbs	None	Fever malaise migratory arthritis signs of under-lying systemic disorder
Erythema induratum	More often in females	Tuberculide le sion panarte ritis and phle bitis affecting arterioles and venules of subcu taneous tissue	History of tuberculosis elsewhere	Pain in lesions	Irregularly shaped ulcer with under mined edge base covered by watery discharge nodules may be present lesion usually on calf	None	Signs of tubercu-losis elsewhere
General ized scler-edema	None	Thickening and hyalinization of collagen bundles deposition of mucin like material	History of progression of stiffening of skin of various portions of body	Stiffening of skin of forearm arm	Changes in skin which becomes waxy to touch	None	Changes observed in back breasts
Dermato myositis		Inflammation of muscle bundles and then muscle destruction	History of relapses and remissions	Muscular weakness tenderness	Dermatitis soft doughy muscles later atrophy of muscles changes limited to groups of muscles	Pulsations in main arteries may be absent oscillo-metric readings reduced	Malaise fever weight loss

Table 17 Rare Vascular Disorders of Extremities

Clinical entity	*Sex or race difference*	*Pathogenesis or pathology*	*Characteristic points in history*	*Symptoms present locally*	*Characteristics of lesion or change in skin*	*Signs of arterial or venous impairment*	*Findings elsewhere in body or systemic reactions*
Acroparesthesia	Predominantly in females over 30 years of age	May be associated with neurologic involvement of spinal cord or vitamin deficiency	Symptoms primarily present during night exposure to cold or exercise reduces pain	Tingling numbness burning in hands or feet	No objective findings	None	Signs of underlying condition
Chronic progressive hypertrophic acrocyanosis	None		Slow progression of disorder	No pain	Hypertrophy of soft parts of hands and feet cyanosis or intense rubor of overlying skin	None	None
Ainhum	Predominantly in Negroes	Strangulation of tissues distal to fibrous band	Slow progression of band-like constriction of toe	Severe pain in involved toe	Linear fibrous band at digitoplantar fold of fifth toe with enlargement and then spontaneous amputation of portion distal to it	None	None
Acrodynia	None	Vitamin deficiency	History of photophobia anorexia irritability	Photophobia and anorexia may be present	Red and puffy hands and feet associated with papular rash	None	None
Chronic pernio	Predominantly in females	Spasm of small vessels of skin producing anoxia	History of appearance of lesions with onset of cold weather and disappearance with onset of warm weather	Burning and itching and then severe pain with appearance of ulcer	Masses on lower third of leg with thinning of skin and appearance of a deep red color followed by formation of ulcers	None	None

bophlebitis since the nodules are not found in the vicinity of superficial veins furthermore they tend to ulcerate The latter point is likewise of value in distinguishing the condition from erythema nodosum (For differentiation from chronic chilblains see p 333 and Table 8 p 78)

Treatment No specific therapy exists and the possibility of controlling the condition with the clinical means at hand is not good As in the case of ulcers of venous origin the ulcerated nodule should be treated with prolonged bed rest, elevation of the limb and hot soaks If tuberculosis is the etiologic factor exposure of the involved lymph nodes to roentgen therapy may be of value In the non tuberculous type general supportive measures should be used and foci of infection should be eliminated A resistant ulcer if limited to a small portion of the limb may be treated by excision and skin grafting The fact that recurrences occur despite treatment contributes to a poor prognosis

AINHUM (DACTYLOLYSIS SPONTANEA)

Ainhum is a disease peculiar to the dark skinned races especially the Negro characterized by the formation of a linear fibrous band at the digitoplantar fold of the fifth toe eventually producing encirclement of the digit (Fig 54) [2] As this structure grows deeper it causes a ring like strangulation of the tissues distal to it associated with pressure atrophy and resorption and frequently a pathologic fracture of the bone Gradually the distal end of the toe becomes enlarged and bulbous to be followed by spontaneous amputation The roentgenographic findings consist of narrowing of the shaft thinning of the cortex of the phalanx pathologic fracture and rotation of the distal phalanx (Fig 54B)

Clinical Characteristics The symptoms of ainhum are limited to the fifth toe on one or both feet there are no systemic reactions As the constriction begins to form some pain may be experienced in the involved digit Later this is almost invariably present and frequently is quite severe Ulceration and inflammatory signs are not noted at the onset of the disease but the former may occur subsequently Symptoms may persist over a period of years

Treatment This consists of a metatarsophalangeal disarticulation with removal of the metatarsal head thus producing relief of symptoms Healing will generally occur If the lesion is not handled surgically nature will do the same thing but more slowly At times the disease can be arrested by early section of the fibrous ring or by division of the skin down to the periosteum on the dorsum of the toe

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Table 17 (continued)

Clinical entity	*Sex or race difference*	*Pathogenesis or pathology*	*Characteristic points in history*	*Symptoms present locally*	*Characteristic of lesion or change in skin*	*Signs of arterial or venous impairment*	*Findings elsewhere in body or systemic reactions*
Acrocyanosis	None	Capillary or venous dilatation due to atony persistent arteriolar spasm	History of discoloration of skin of extremities	None	Persistent cyanotic rubor of skin of hands and feet	None	None
Livedo reticularis	None	Marked vasospasm of small cutaneous vessels	History of mottling of skin	None	Reticular bluish discoloration of skin	None	None
Erythromelalgia	None	Marked vasodilatation during attack	History of attacks of burning sensation in extremities on exposure to a warm environment or with rise in body temperature	Severe burning pain in hands or feet during attack	Redness and warmth of skin of hands and feet during attack	Bounding pulses and increase in oscillometric readings during attack	None

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CHAPTER

XXII DISORDERS OF THE LYMPHATIC SYSTEM

The disorders affecting the lymphatic system are much less readily classified than those of either the arterial or venous systems Frequently, the condition appears insidiously making it difficult to identify the etiologic agent Lymphatic ob truction may be due either to intrinsic structural abnormalities of the lymphatic system or to metastatic invasion injury or inflammation of the lymph channels and nodes The predominant finding is nonpitting swelling of the limb as a result of lymph stasis

PRIMARY LYMPHEDEMA

Congenital Lymphedema

Simple Congenital Lymphedema (*Lymphangiectasia Congenita*) This is one of the more common types of congenital lymphedema It is characterized by diffuse swelling of the leg appearing at birth (Fig 55) There is no familial or hereditary tendency The skin and underlying structures are thickened the fat being replaced by greatly dilated lymphatic spaces surrounded by fibrous tissue The cause for these changes is not known, although it is probably some type of developmental anomaly

Chronic Hereditary Lymphedema (*Milroy s Disease*) This is a rare condition which is similar in all respects to simple congenital lymphedema except for the fact that more than one member of a family will be found suffering from it The swelling is painless circumscribed and usually limited to the legs It sometimes pits on pressure but it is firmer than ordinary edema It is a chronic disorder having no effect on the general health of the patient Although originally lymph edematous eventually the process becomes one of a dense fibrous tissue reaction

Lymphedema Praecox

Primary idiopathic lymphedema or lymphedema praecox generally appears in girls around the time of puberty Because of this relationship an endocrine factor has been proposed as an etiologic agent Another possibility is a congenital alteration of lymphatic vessels The histologic changes are analogous to those occurring in the capillaries and venules of a venous nevus

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FIG 56 Lymphedema of left lower extremity following metastasis of fibrosarcoma of fifth toe to inguinal lymph nodes

sense of heaviness and a feeling of stretching of the skin the patient experiences no symptoms in the swollen extremity However the distorted appearance frequently causes emotional trauma

SECONDARY LYMPHEDEMA

Lymphedema may be secondary to a number of different conditions in which there is interference with the movement of lymph out of an extremity resulting in lymph stasis The etiologic agent may be obstruction of lymph channels by

Clinically lymphedema praecox is characterized by the slow development of swelling of one or both lower extremities This may first take the form of some puffiness about the ankle which then spreads upward onto the leg eventually to involve the entire limb However, in many instances the change is limited to the foot and ankle or it may reach as far as the knee At the onset the degree of edema appears to be increased by such factors as prolonged physical activity



Fig 55 Simple congenital lymphedema of left lower extremity

in the upright position the menstrual period and hot weather At this stage bed rest causes the swelling to decrease or disappear entirely by morning As the condition progresses the accumulation of fluid during the day becomes greater while the effect of recumbency on reducing it is much less marked Although cutaneous ulcerations occur rarely the leg is susceptible to attacks of acute lymphangitis These may be noted while the process is developing to disappear after a stationary state in the size of the limb has been reached Aside from a

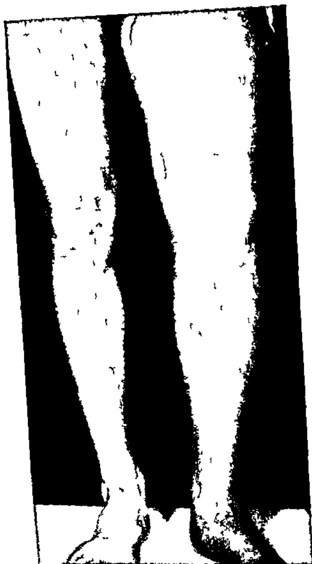


Fig 56 Lymphedema of left lower extremity following metastasis of fibrosarcoma of fifth toe to inguinal lymph nodes

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SECONDARY LYMPHEDEMA

Lymphedema may be secondary to a number of different conditions in which there is interference with the movement of lymph out of an extremity, resulting in lymph stasis The etiologic agent may be obstruction of lymph channels by

tumor cells, destruction of the continuity of the lymphatic system, or a lymph angitis followed by thrombosis

Malignant Occlusion

Metastasis of malignant tumors to regional or distant *lymph nodes and lymph* channels may initiate lymphedema of a limb In a woman with involvement of one lower extremity, the primary site of the neoplasm is generally in the genital tract, the tumor ordinarily being slow growing and not found upon vaginal examination This is so even at a time when metastasis to the inguinal lymph nodes has already occurred In a man with unilateral lower extremity lymphedema, the prostate gland and the bladder must always be considered as a possible source of the malignancy Hodgkin s disease lymphosar coma and fibrosarcoma (Fig 56) may also be associated with lymphedema of a limb

The swelling associated with metastasis is slow, progressive, and painless It is present initially in the proximal portion of the limb and later distally The skin becomes hard and indurated and gives the appearance of being firmly adherent to the subcutaneous tissues A prolonged period of bed rest with the extremity elevated will cause only slight reduction in the edema



Fig 57 Lymphedema following extensive destruction of lymphatic channels by shell fragment wound of leg

Destruction of Continuity of the Local Lymphatic System

Removal of the local lymph nodes or de struction of the lymph channels will frequently produce lymphedema Such a situation may follow extirpation of the regional lymph nodes in the control of tuberculosis or of malignant disease It may also occur after extensive injury to a limb if a sufficient number of lymphatic channels are severed (Fig 57) More difficult to explain is the lymphedema which *on occasion is associated with minimal trauma Evidently under such circum* stances the normal process of repair fails and a disorder of the lymphatic system is initiated at the site of the injury This may spread up and down the limb causing either an impairment of lymphatic return or an increased output of lymph [9]

An example of lymphedema following surgical treatment of metastasis to lymph nodes is the swelling of the arm associated with radical mastectomy for carcinoma This is a relatively frequent *finding and a very disabling sequel of the operation*

In the majority of instances it appears between the third and sixth month after surgery although on occasion it may not occur for five or more years The edema may be brawny with thickening of the skin or soft with thin shiny skin Generally it is persistent and progressive eventually producing a markedly enlarged upper extremity In some cases it is reduced by rest and elevation of the limb and increased by dependency while in others these measures fail to have any effect Pain may be associated with the swelling being due either to the increased tension of the edematous tissues or to direct involvement of the brachial plexus by the malignant process[3, 10] It should be emphasized that besides the removal of lymph nodes and destruction of lymph channels there are other factors such as venous obstruction postirradiation fibrosis and infection (see below) that may be implicated in the production of the lymphedema[3, 10]

Inflammatory Lymphedema

Repeated attacks of cellulitis in the extremities particularly in the feet are frequently followed by the appearance of lymphedema involving the distal portion of the limb The swelling is due to capillary lymphangitis of a widespread nature Drainage of the infection into the regional lymph nodes with a consequent inflammatory reaction also contributes to the difficulty of removing lymph fluid Persistent lymphedema is due to thrombosis of the involved lymph channels from the numerous inflammatory episodes the resulting lymph stasis causing further fibrosis of patent vessels and hence accentuation of the *process*

The clinical story associated with the *common* type of inflammatory lymph edema produced by a streptococcal infection is fairly characteristic A history is obtained of a sudden onset of cellulitis of the foot and lymphangitis associated with a high fever chills and other signs of a marked systemic response Examination during such an acute phase reveals a red hot and swollen portion of the limb with typical findings of involvement of the lymphatic channels and tenderness and swelling *of the regional* lymph nodes With treatment (p ,66) the temperature generally falls to normal within 2 or 3 days while the local changes subside much more slowly sometimes remaining for as long as [illegible] weeks Each [illegible] a little more residual swell[illegible] between the acute episodes [illegible]

The etiologic agent for the recurrent attacks of cellulitis may vary In some instances it can not be identified despite careful examination In others dermatophytosis of the toes is either directly responsible or indirectly implicated by facilitating the secondary invasion into the tissues Injuries such as a minor scratch by a fish bone a penetrating wound or a burn may cause extensive lymphangitis and at times even after a single attack permanent lymphedema of a marked degree The acute inflammation may not be noted for weeks or months after the skin was first traumatized the explanation for the delay is not clear

Various systemic disorders may also lead to repeated attacks of cellulitis and lymphangitis followed by lymphedema Among these are influenza pneumonia malaria and filariasis In filariasis the question arises as to whether the recurrent episodes are due to this disorder or to secondary *infection* There is little doubt

that the initial attack is of filarial origin, the lymphangitis probably being a manifestation of a foreign protein reaction either to some metabolic by product of the adult worm or to its body constituents It is of interest that this inflammatory response is of a descending rather than of the usual ascending type In contrast, the subsequent attacks generally resemble a streptococcal infection as described above It is these that are followed by the appearance of the typical brawny induration (elephantiasis) commonly present in the long standing case of filariasis On the other hand the fact that early removal of the patient from an endemic area results in complete disappearance of all clinical findings would support the view that recurrent filarial infections are in some way necessary for the production of the lymphedematous changes in the skin

Aside from those factors which have already been mentioned as responsible for the lymphedema associated with radical mastectomy, the possibility of repeated attacks of cellulitis must also be considered The etiologic agent may be infection either in the operative field or in ulceration of the skin due to recurrent carcinoma However, there must be persistent or numerous episodes of this type, involving the soft tissues of the arm, axilla, and shoulder, before sufficient lymphatic obstruction occurs to produce lymphedema [3, 10]

Differential Diagnosis of Lymphedema

Differentiation from Other Types of Limb Enlargement

In the differential diagnosis of lymphedema it is necessary to consider the various entities which produce enlargement of a limb Since for the most part this subject is discussed in detail in Chapter VI only a resume will be presented here *The fact that persistent lymphedema is generally associated with definite alterations in texture and consistency of the skin and that these changes are unaffected by elevation of the limb is of importance in distinguishing this type of swelling from that due to systemic disorders or to local venous or arterial impairment* However a word of caution is required First if the lymphedema is minimal or if it has not been present for any period of time, the characteristic changes in the skin may be absent Second venous edema if left unchecked may result in an indurated brawny and hypertrophied limb which resembles that found in true lymphedema Under these circumstances other diagnostic tests must be made (p 408)

Unilateral lymphedema may be mimicked by a number of different conditions For example in congenital arteriovenous fistula there may be an enlargement of the diameter of the involved limb At the same time however it is also increased in length, a finding which is not noted in true lymphedema The swelling that accompanies acute deep thrombophlebitis of one lower extremity should pose little difficulty in differential diagnosis, in view of the suddenness of onset and the associated systemic and local changes (Chap XIV) Unilateral postphlebitic edema may require a more extensive examination particularly if secondary lymphedematous changes have already occurred (see above) Certainly the various systemic conditions such as congestive heart failure nephrosis, myxedema and nutritional disorders can be ruled out as etiologic

factors, since they are almost always characterized by swelling of both lower extremities

If the lymphedema is bilateral then the differentiation must include several other entities besides the systemic diseases mentioned above Among these is lipodystrophy (lipedema) which is a painless insidious enlargement of the lower extremities frequently encountered in women Although the swelling increases somewhat both in hot weather and with prolonged assumption of the upright position it is not particularly affected by elevation of the limb nor does it pit readily The disorder is invariably noted in obese individuals which is a distinguishing point from lymphedema since such a relationship does not necessarily exist in this condition Of diagnostic value on occasion is the x ray finding of trabeculations in the soft tissues of the lymphedematous limb[a] and the absence of such a change in lipodystrophy

Differentiation of Various Entities Producing Lymphedema

Aside from the differentiation of lymphedema from other types of swelling it is also essential to determine which of the disorders of the lymphatic system is responsible for the abnormality In this regard the history of the appearance of diffuse enlargement of a part or an entire limb at birth or soon after places the condition in the category of congenital lymphedema If the changes are first noted around puberty then the best possibility is lymphedema praecox In neither of these two groups should there be a history of the existence of any of the common etiologic agents responsible for secondary lymphedema On the other hand for the proper diagnosis of the latter one of these must be identified

TREATMENT OF LYMPHEDEMA

Since the general measures in the control of both primary and secondary lymphedema are the same it is considered advisable to discuss the entire problem in th ...

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Medical Therapy

Control of Swelling The primary purpo e in the treatment of lymphedema is the prevention of the accumulation of the fluid in the limb If this is not accomplished early in the disease ...

fibroblastic infiltrati ... f

The resulting fibroe ... for the most part resistant to medical measures

The approach to the problem of maintaining the lower limb relatively free of swelling involves first a period of bed rest with the leg elevated at a 45° angle through a sling and then the use of various means ...

... bandage (see Appendix)

cm (3 inches) wide, is much more effective in controlling the edema The foot and leg are first covered by a cotton stocking and then the bandage is wound around the extremity like an Ace bandage It should be removed in the afternoon and reapplied but not exactly superimposed, so as to minimize ridging The degree of tautness can only be determined by trial and error If the bandage is too loose it will not prevent the accumulation of fluid during the day, while if too tight it will cause discomfort and even pain At night the patient should always sleep with the foot of the bed elevated 6–8 inches As an adjunct to the above steps, means to remove salt from the body may be of value This involves placing the patient on a salt poor diet and having him take one of the oral mercurial products daily Parenteral mercurials given at intervals are also useful

Prophylaxis in Regard to Acute Inflammation In order to prevent further attacks of cellulitis and lymphangitis, all types of infections of the skin should be avoided Dermatophytosis, particularly, should be carefully controlled and eliminated Aside from the usual measures (p 196), it may be worthwhile to obtain a culture of the offending fungus so that an autogenous vaccine can be produced

Therapy for Recurrence of Acute Inflammation For the treatment of a recurrence of cellulitis and lymphangitis it is always necessary to utilize antibacterial agents parenterally Generally penicillin is quite effective in lowering the fever and preventing progression of the condition However, the same precautions should be taken in its administration as when it is given for the control of the systemic reactions occasionally associated with the acute inflammatory stage of dermatophytosis (p 196) Under both circumstances the patient may already be sensitized to a mold and hence the use of a mold extract may elicit an allergic response

Local therapy should be combined with the above measures Wet heat* is useful in localizing the process and in reducing the lymphangitis and lymphadenitis If there is an associated exacerbation of the dermatophytosis appropriate steps should be instituted to control it

Therapy in Postmastectomy Lymphedema Because of the relative frequency of this state, its control deserves special mention The most important step is prophylaxis, during and immediately after the surgical procedure Obstructive fibrosis can be reduced by the use of fine nonabsorbable suture material and by steps to decrease accumulation of serum in the wound[1] Care in making the original incision, so as to prevent the subsequent scar from extending to the arm, and minimum exposure of the limb to postoperative irradiation are also worthwhile precautions The routine and continuous application of a snug compression bandage to the extremity for eight weeks following surgery will likewise help discourage edema formation[7] The limb is wrapped from the distal flexor crease of the palm to as high as the breast dressing will permit the arm being bound to the chest by a modified Velpeau bandage until the fourth postoperative day and by an elastic compression bandage thereafter

Once postmastectomy edema has been formed measures to combat it include

* Before this is attempted the existence of a normal arterial circulation in the limb must be determined

prolonged elevation of the limb * A well fitting glove, to the third finger of which the end of a rope has been sewed is placed over the hand before retiring The other end of the rope is run over a pulley on a Balkan fracture frame, then horizontally for several feet and finally over a second pulley to a counterweight [4] To prevent the reaccumulation of fluid that has drained out during the night a heavy elastic sleeve is fitted snugly around the limb in the morning Massage for 10 minutes twice a day is also useful in this regard

Surgical Therapy

Among the surgical procedures is the placing of silk threads strips of fascia or cellophane in the subcutaneous tissue of the thigh and anterior abdominal wall for the purpose of producing the growth of new lymphatic channels along the course of the foreign bodies In most instances the measures have not been successful

The Kondoleon operation[5] has produced variable results in the hands of different surgeons The method consists of removing wide strips of deep fascia through long lateral skin incisions upon both sides of the leg sections of the overlying edematous fatty tissue being excised at the same time In this manner the musculature is exposed so that anastomosis between supra aponeurotic and infra aponeurotic lymphatics is facilitated The wounds are sutured without drainage to allow the skin to be in direct contact with the underlying muscles For the most part the procedure should be used only when all other means have failed to control the lymphedema

FIBROEDEMA (ELEPHANTIASIS)

If the attacks of cellulitis and lymphangitis in the extremity manifesting lymphedema continue uncontrolled eventually diffuse fibrosis of the skin and subcutaneous tissue and hyperplasia of the lymph vessels will occur [6] These irreversible reactions will enlarge and deform the entire limb except possibly the sole of the foot As the lymphangitic process recurs more and more lymph channels become thrombosed until eventually very few remain patent At this stage the attacks of lymphangitis usually disappear

Clinical Course The clinical story of nonparasitic elephantiasis is similar in many regards to that of inflammatory lymphedema except that the local and systemic responses are generally *more marked* There may be vomiting chills and fever as high as 40 or 41 1 C (105 or 106 F) The inflamed area becomes swollen feels brawny and does not pit on pressure while the regional lymph nodes are enlarged and tender Although the signs of inflammation may subside within several days to a *few weeks* the changes in the skin persist The attacks may recur at frequent intervals *each* time causing greater hypertrophy of the involved tissues The fibrous changes produce ...

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of the leg, which, at times, are the sites of ulceration and subsequent portals of entry for reinfection Pain may or may not be present in the involved limb between episodes of local inflammation and systemic responses If it does not exist, the only complaint may be a sense of heaviness in the leg and difficulty in standing or walking

Treatment The therapeutic results in fibroedema are generally much less satisfactory than in the case of swelling of venous or lymphatic origin In contrast to the latter two states, fibroedema is not affected even by a prolonged period of bed rest Nor is the condition benefited by any of the procedures devised to increase lymphatic drainage The only means left to treat the unsightly, large, almost useless, limb is to excise all the tissues of the leg between the skin and subaponeurotic structures The skin should also be excised if it is in a poor state of viability, in which case skin grafting will be required The rationale for the operation is the removal of tissues in which fluid might accumulate[4] At times it may even be necessary to amputate the extremity

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CHAPTER

XXIII CONGENITAL ANOMALIES

CONGENITAL ARTERIOVENOUS FISTULA

In congenital arteriovenous fistula or aneurysm there are multiple communications of small caliber between the arterial and venous systems locally, unassociated with any antecedent trauma. The condition represents a persistence of connections which exist at the beginning of the process of differentiation of arteries and veins from a common embryologic anlage. It is found most often in the extremities (Fig. 58) but may be present elsewhere.

Recently a new syndrome of "arterial varices" has been described[8] which is considered to be a modification of a congenital arteriovenous fistula but which clinically resembles primary varicosities. In this disorder it is believed that communications between the arterial and venous systems in the lower limbs which had been present during fetal life but closed prior to birth are reopened as a result of some physical change occurring during or after puberty. Due to the movement of blood from the large arterial trunk through multiple connections into the venous system, the superficial veins and their branches dilate rapidly, and as a consequence, the valves become incompetent. (For differentiation from primary varicosities see *Differential Diagnosis* of varicosities, Chap. XIII.)

Clinical Characteristics

A congenital arteriovenous fistula may be present for many years before complaints develop, probably because progressive enlargement of the communications must first take place.[1] Even then there are no real difficulties other than a sense of discomfort and an awareness of the local or diffuse enlargement of the limb. However, if the lesion begins to grow rapidly, pain may be experienced as a result of pressure on neighboring nervous elements. After many years there may appear symptoms of cardiac impairment and later failure.

Physical examination reveals variable-sized masses (Fig. 58) which ordinarily do not exhibit the characteristic systole bruit and thrill found in the traumatic type of arteriovenous fistula (Chap. XVII). The lack of such findings is probably due to the fact that although there are many communications between the local arterial and venous systems, they are generally extremely small. At times visible venous pulsations may be noted, while varicose veins are almost invariably

present The involved limb may be longer and larger in circumference than the opposite extremity, thus indicating that the fistula was functioning even before the epiphyseal centers were closed As in traumatic arteriovenous fistula the skin



Fig 58 Congenital arteriovenous aneurysm A Aneurysm involving lower portion of forearm B Aneurysm involving only fifth finger of right hand

temperature proximal to the lesion is high due to the greater flow of blood through the cutaneous vessels There may also be an increased growth of hair on the limb and excessive sweating Commonly, a congenital arteriovenous fistula is associated with different types of hemangiomas

With regard to laboratory procedures a study of the oxygen content of blood

obtained from veins proximal to the lesion generally reveals readings approaching those obtained from arterial blood Arteriography is likewise helpful in confirming the diagnosis (Chap XXV)

TREATMENT

The treatment is, for the most part surgical This consists of extirpation of the lesion which is an extensive procedure even under the most propitious circumstances Attempts must be made to remove all the tissues in which communications exist involving tedious dissection and ligation of many bleeding points When the entire limb is affected with numerous communications traversing the muscles and other structures excision becomes impracticable and hence either the fistula is left alone or the limb is amputated Involvement of a single digit (Fig 58B) is best treated by amputation

Among other methods of therapy that have been tried are the use of radium and the injection of superficial veins with sclerosing solutions The application of a rubber bandage to the limb to maintain the superficial vessels in a collapsed state is of value in preventing some of the cardiovascular complications of an arteriovenous fistula Under these circumstances less blood enters the veins from the arterial system through the abnormal communications and hence venous return to the heart is reduced

In the treatment of arterial varices in the leg the great saphenous vein and its branches are exposed in the groin and all connections from the arterial or venous side are dissected free and widely excised a 4 inch segment of great saphenous vein is also removed[8] All incompetent venous communicating points and secondary arterial connections are excised Finally the large veins on the lateral aspect of the leg or in the popliteal space are removed

VASCULAR TUMORS

A discussion of congenital vascular tumors involving relatively superficial sites offers certain difficulties since no generally accepted classification of these conditions exists Furthermore in several instances many terms are used clinically to designate the same syndrome

Tumors composed of blood vessels whether benign or malignant always contain two or more tissue types[11] Basically they consist of tubes lined by endothelia enclosed within a sheath of connective tissue fibers In addition other cellular structures may be present such as smooth muscle pericytes fat nerves and bone

TELANGIECTASIA

Telangiectasia is an acquired dilatation of capillaries and small venules of the skin which first appears in adulthood It may result from exposure to wind or sun or it may form after treatment with radium or x ray It is also present in a number of different dermatologic conditions such as acne rosacea lupus erythematosus and syphilis Several of the more common disorders characterized by telangiectasia will be briefly discussed below

Clinical Entities

Spider Nevus This lesion consists of a central, raised, dilated vessel with radiating tributaries which is found in the skin of the face neck, thorax dorsum of the hands (Fig 59), and elsewhere Pressure on a spider nevus causes it to



Fig 59 Spider nevi on dorsum of hand associated with cirrhosis of the liver)

blanch The entity recently received considerable attention because of its apparent close relationship to liver disease It has also been noted during pregnancy generally disappearing after delivery and in the absence of any underlying disease The condition may appear at any age but it usually develops during adult life

Senile Ectasia (*Senile Vascular Nevus*) This condition consists of multiple, bright red papules noted on the extremities as well as the trunk and elsewhere, [illegible] The lesions represent tufts [illegible] o their presence

[illegible] Weber's Disease) This condition is characterized by multiple slightly raised small telangiectatic lesions of the skin mucous membranes and viscera It appears to have a definite familial incidence The lesions made up of dilated capillaries with thin walls and covered by a thinned-out skin or mucous membrane are most commonly found in the nose Less frequent sites are the tongue lips, cheeks fingers and hands Pulmonary arteriovenous fistulas may be noted in conjunction with this disorder (Chap XXIV)

Hemorrhage particularly from the nose, mouth and gastrointestinal tract frequently occurs This tendency increases with age and may produce a severe anemia As with spider nevi pressure on the lesions causes them to disappear Of further importance in diagnosis are the familial history and the absence of any defects in the clotting mechanism Treatment consists of destroying the tumor by electrocoagulation or some other method



FIG 60 Hemangioma of *right arm* made more apparent by use of infrared photography

Pulsating Telangiectasia This condition is similar to a spider nevus and is associated with cirrhosis as well as other types of severe hepatic involvement Of interest is the fact that *pulsations* can be seen in the lesions They may be found on the face trunks and hands

HEMANGIOMAS

Hemangioma is probably a congenital growth of tissue in which blood channels form It the most common neopla m of infancy and childhood and is frequently evident at birth The condition is noted much more often in females than in males The tumor may vary in size from tiny flecks to lesions involving an entire half of the body (Fig 60) On occasion it may be found in skeletal muscle[10] Hemangiomas tend to grow slowly and generally cease enlarging when adulthood is reached Microscopically endothelial lined spaces of varying sizes are found surrounded by interstitial connecti e tis ue[4] The proportion of lipoid and fibrous tissue in the tumor will determine its consistency

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blanch The entity recently received considerable attention because of its apparent close relationship to liver disease It has also been noted during pregnancy generally disappearing after delivery and in the absence of any underlying disease The condition may appear at any age, but it usually develops during adult life

heaviness and aching particularly if the patient stands for any period of time

Diffuse Hemangioma This rare vascular tumor may affect a large part of an entire extremity The involved limb is generally enlarged and discolored at birth and progressively increases in size The lesion consists of great numbers of dilated blood sinuses resembling varicose veins Elevation of the extremity tends to decrease its size due to collapse of the vascular channels in this position A sense of heaviness and aching may be present in the limb on standing or walking The condition may be associated with other congenital anomalies such as nevus venosus *and congenital* arteriovenous fistula

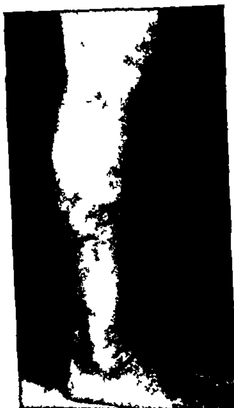


FIG 61 Phlebectasia a congenital vascular anomaly

Treatment of Hemangiomas

The selection of appropriate therapeutic measures depends upon the size and location of the tumor The capillary hemangioma and the port wine stain may sometimes be effectively treated by destroying the capillaries in the surface layer of the skin through rubbing with sand paper or application of dry ice Cosmetic camouflages are also worthwhile especially the use of tatooing It is well to remember however that both capillary and cavernous hemangiomas appear at birth or shortly thereafter grow quite rapidly to attain a maximum size and then in some instances may undergo *spontaneous involution* by the age of 6 years It is therefore advisable to delay treatment until after that period

In the case of encapsulated hemangiomas of the skin and subcutaneous tissue complete surgical excision with plastic closure is the best therapeutic approach, this being more readily carried out in the case of lesions on the extremities than elsewhere Intravascular injection of sclerosing solutions with or without vascular ligation is also helpful in the treatment of large hemangiomas Irradiation of the lesion should be undertaken with caution [7] since it may produce atrophy and *telangiectasia of the skin and* may disturb bone growth

PHLEBECTASIA (VENOUS ANOMALIES)

Phlebectasia is a congenital vascular anomaly in which there is significant enlargement and fusiform dilatation of venous channels in an extremity without any demonstrable evidence of abnormal arteriovenous communications It has been considered as a variant of a cavernous hemangioma

Because the lesion can be compressed, hemangioma must be differentiated from such conditions as large dilated varices, lymphangiomas, and lipomas.[4] Extensive varicosities are readily emptied by elevation of the limb, while further confirmation for the diagnosis can be obtained by the use of the tests for incompetency of venous valves (Chap. V). A lymphangioma may be compressible, but this response occurs less readily than in the case of a hemangioma, and the return to the previous shape is much slower. Differentiation from a lipoma may be difficult, particularly when there is a considerable deposition of fat about the vascular channels of the hemangioma. In fact, in some instances it is necessary to incise the tumor and demonstrate the vascular spaces before arriving at the correct diagnosis.[4]

Clinical Entities

Nevus Venosus (Port-wine Stain, Birthmark). This is one of the most common hemangiomas. It is made up of numerous dilated capillaries that lie flush with the surface of the skin. The tumor appears as a red or purple area of erythema which blanches readily on pressure. It may vary in size and be single or multiple. It is most commonly located on the side of the face or neck, although it may also be noted on the trunk and extremities. The lesions are almost always present at birth and rarely enlarge afterward. In fact, in many instances they gradually disappear.

Capillary Hemangioma (Strawberry Nevus, Capillary Nevus, Plexiform Angioma). This lesion is by far the commonest histologic variety of vascular tumor.[11] Most frequently it has the appearance of a circumscribed, bright red or purple warty projection of the skin. Although it infiltrates tissues and may exhibit persistent growth, it is benign in the sense that it does not metastasize. Its most frequent location is in the skin of the face and neck, and is rare elsewhere. Histologically it is composed of closely packed simple narrow capillary tubes lined with differentiated endothelium and surrounded by a sheath of delicate reticulum fibers.[11] The capillary network may be scattered diffusely through otherwise normal tissue.

Cavernous Hemangioma (Nevus Cavernosus). This tumor is similar to the capillary hemangioma except that the majority of the vessels forming it are widely dilated. It consists of masses of thin-walled sinuses lined with endothelium and filled with blood. Although usually present at birth, a cavernous hemangioma may not be obvious until later in life. The nodules grow slowly and may eventually become quite large. However, as in capillary hemangioma, the tumor is considered benign since it does not metastasize. It is found on the extremities, involving the skin, subcutaneous tissue, and muscle, and also on the face and neck and in the viscera.

The cavernous hemangioma consists of irregular, soft, and poorly circumscribed single or multiple nodules with a cyanotic or purplish-red hue. It may be flat, elevated, or warty in appearance, or it may resemble superficial dilated veins. Raising the limb reduces the amount of blood in the tumor, thus making it somewhat smaller. If of considerable size, the lesion may produce symptoms of

into the cutis from local dilated and engorged vessels Then a predominance of lymphocytoid cells of Marchand appear these apparently arising from the walls of the blood vessels Later there is a proliferation of the endothelium of the blood vessels together with the formation of new but imperfect capillaries and an increase in lymphocytes plasma cells and mast cells The microscopic picture then becomes that of an angiosarcoma or fibrosarcoma

Initially the lesion is a bluish red or reddish brown well-demarcated macule on the extremities varying from a few millimeters to a few centimeters in diameter Then it slowly becomes elevated multiplies and coalesces to form indurated bluish black plaques (Fig 62) As the subcutaneous tissue becomes diffusely infiltrated by the hemorrhagic verrucous lesions marked edema of the involved limb occurs ultimately followed by elephantiasis In some patients the swelling may precede the skin manifestations by long intervals Arthralgias are common and visceral involvement is present in about 10 per cent of cases[9] In all instances the clinical diagnosis of Kaposi s sarcoma should be confirmed by histologic studies since a number of conditions may simulate it Among these are lymphoblastomas true angiosarcomas and circulatory disturbances especially those of venous and lymphatic origin

After a variable course ranging from a few months to 25 years death takes place generally from progressive cachexia or hemorrhage from friable tumors in the gastrointestinal tract or the lungs[3] The only therapy worth a clinical trial is the use of roentgen rays This approach is only palliative but it may prolong life for years

ANGIOSARCOMA

Angiosarcoma is another malignant tumor which has a tendency to occur on the extremities It appears more frequently in childhood and youth and affects both sexes equally The initial lesion usually is a solitary firm bulky tumor deep in the soft tissues Pain and tenderness may be present as a result of pressure of the mass on nervous elements As in the case of Kaposi s sarcoma edema of the extremities is frequently present

GLOMUS TUMOR

The glomus tumor is a congenital vascular anomaly which represents a pathologic alteration of the glomus (p 412) It is generally found in the nail beds of the fingers and toes in the palm of the hand and in the sole of the foot and less frequently in the forearm the area around the knee the arm the leg the scapular region and the thoracic wall Histologically the tumor demonstrates an overgrowth of the vascular spaces and of epithelioid cells normally found in the glomus A network of nonmedullated nerve fibers and many Pacinian corpuscles are usually noted in the collagenous reticulum

Clinical Characteristics

The most outstanding symptom is the exquisite sharp and burning pain present in the region of the lesion and radiating up the entire extremity The complaint is initiated by distension of the numerous venous channels of the tumor mass

The clinical picture is by no means characteristic The patient may complain of a sensation of heaviness, aching tenseness and fatigue in the involved limb elicited by *physical effort* Numerous superficial thin walled vascular structures (Fig 61) give the extremity a cyanotic appearance Elevation of the limb collapses the venous structures at the same level as in the normal side, thus indicating grossly that the venous pressure in the prominent channels is not increased That these are dilated venous sinusoids can be demonstrated by the use of venography Furthermore, there are no abnormal pulsations thrills or bruits to suggest arterial connections

Although the above findings are of value in differentiating phlebectasia from congenital arteriovenous fistula at times the resemblance may be so great that



Fig 62 Lesions of the toes produced by Kaposi s sarcoma

arteriography and oxygen determinations are necessary to make the correct diagnosis On the other hand little difficulty should be experienced in distinguishing phlebectasia from varicosities In the latter the veins are usually uniformly dilated and tortuous and conform to the normal anatomic distribution [1]

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi

Kaposi s sarcoma is a relatively rare malignant tumor of blood vessel origin characterized by the successive appearance of vascular lesions most commonly located in the skin of the extremities and less often in the mucosa lymph nodes viscera, and elsewhere About 90 per cent of the cases occur in men generally after the age of 40 years The etiology and the nature of the disease are not known but there appears to be some relationship to the reticuloendothelial system The condition is considered to be a true but atypical sarcoma of low grade malignancy

Early, the histologic picture of Kaposi s sarcoma is that of an inflammatory response rather than of a neoplastic process [6] The changes follow hemorrhage

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by blood, thus causing pressure on the rich plexus of small nerve fibrils The pain may appear spontaneously or it may be produced by exposure of the affected part to extremes of cold or heat, particularly the latter Occasionally the slightest pressure from clothing or bed clothes will precipitate a paroxysmal attack of agonizing pain The fear of such discomfort may influence the patient to adopt certain protective habits which eventually will result in actual atrophy of disuse of the entire extremity [9] Elevation of the involved limb and the sudden application of an arterial occlusion pressure will relieve the pain,- since under these circum stances distension of the vascular tumor is prevented

Examination generally reveals a subcutaneous or subungual mass varying from 0 5 to nearly 3 cm in diameter deep red to purple or blue in color and sharply demarcated from the surrounding tissues At times it may not be visible or palpable

Treatment

Since the glomus tumor is benign surgical extirpation results in an immediate cure However, on occasion, the area of radiation of the original pain may persist for several months When the tumor is entirely removed there will be no recur rences In this regard it is always necessary to palpate the involved site very care fully at the time of operation, since multiple grouped tumors are sometimes present

LYMPHATIC TUMORS

Tumors of lymph vessels are seen much less frequently than those of blood vessels They can be divided into the simple, the cavernous and the cystic [13] The simple type which is usually congenital consists of small well defined lesions, made up of large networks of lymphatic spaces *into which lymphatic channels* enter The tumor is located on the skin as well as on the mucous membrane and is slow growing

The cavernous lymphangioma is also congenital appearing at birth or shortly afterward and growing slowly Histologically it is made up of large dilated lym phatic channels containing lymph and at times some blood The lesions are generally found in the skin and subcutaneous tissue However they may also be located on the tongue, lips and cheeks causing great enlargement of these structures

Cystic lymphangioma or hygroma is considered to develop from embryonal rests - It is usually composed of several cysts lined with endothelium and con taining serous fluid or lymph The tumor is generally found in the neck and less frequently in the axilla groin and pelvis It is readily compressible

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side, in some instances both temporal arteries become involved The condition may spread to neighboring vessels including the retinal and even the cerebral arteries In one third or more cases there is a significant degree of visual impairment which is generally permanent and may be severe enough to cause total blindness Despite such abnormalities fundal changes are surprisingly insignificant

The diagnosis is made upon prodromal systemic complaints followed by localizing findings in the region of the superficial temporal artery In doubtful cases a biopsy of the vessel may have to be performed Among the local conditions which must first be eliminated as a possible cause for headaches associated with fever is sinusitis

Treatment Since temporal arteritis usually runs a self limiting course of approximately seven months it is difficult to evaluate the various procedures which have been advocated as therapy Headaches have been relieved by infiltration of the artery with procaine In some cases excision of the involved segment of vessel has been beneficial Salicylates appear to be the most effective analgesic agents Antibiotics are of little value Recently ACTH and cortisone have been used with dramatic improvement although in some instances relapse occurred when the medication was stopped [9] It would appear that prolonged therapy of this type is indicated Although the belief commonly held is that temporal arteritis is a nonfatal disease it is possible that longer follow up studies may modify this view

ANEURYSMS OF THE THORACIC AND ABDOMINAL AORTA*

In recent years aneurysms of the thoracic and abdominal aorta have been observed with increasing frequency This is probably because of greater accuracy in diagnosis and because of the greater incidence of degenerative diseases resulting from a longer life expectancy The types of aneurysms seen in the aorta in its course through the thorax and abdomen are similar to those located in the arteries of the extremities namely the true and the false sacs (See *Traumatic Arterial Aneurysm* Chap XVII)

Etiologic Factors Most aortic aneurysms are caused either by syphilis or by arteriosclerosis Occasionally mycotic embolism polyarteritis nodosa trauma and chronic infections such as a tuberculous abscess in contact with the aorta may be etiologic factors These agents appear to operate in different sites For the most part arteriosclerotic aneurysms are located in the terminal portion of the abdominal aorta below the origin of the renal arteries (Fig 63A) Syphilitic aneurysms occur predominantly in the thoracic aorta (Fig 63B) although infrequently they are noted in the abdominal aorta above the level of the renal arteries The usual sites of aneurysmal formation due to trauma are either in the first portion of the ascending aorta or the beginning of the descending aorta just distal to the ligamentum arteriosum Both these locations are comparatively fixed points which may be the explanation for their vulnerability to trauma

* For sudden or insidious occlusion of the aortic bifurcation see Chap X

CHAPTER XXIV PERIPHERAL VASCULAR ENTITIES NOT AFFECTING THE EXTREMITIES

Vascular disorders of the lungs, brain abdominal viscera face and chest wall rightfully belong in the category of peripheral vascular diseases However to present a detailed discussion of each of these subdivisions would expand this volume beyond reason Therefore it seems advisable here to describe only briefly some of the more common of these conditions and to give references to original material if a fuller description is desired

TEMPORAL ARTERITIS

Temporal arteritis is a rare vascular disorder first described as a clinical entity in 1932 [19] which affects elderly patients primarily women In view of the systemic responses the possibility of infection as an etiologic factor has been suggested but no definite evidence to support this view has been forthcoming The condition is considered to be a generalized chronic arteritis, although the lesion in the temporal artery receives the most attention in the diagnosis

Pathology The pathologic picture is one of panarteritis Grossly the temporal *artery is relatively firm and rigid and the lumen is small or sometimes completely* occluded by a thrombus or by endothelial proliferation Histologically the intima is found to be greatly thickened while the media for the most part is destroyed and replaced by granulomatous tissue containing multinuclear giant cells [10] Infiltration with lymphocytes and plasma cells is present both in the media and adventitia particularly around the vasa vasorum of the latter Fibrosis may also be noted

Clinical Characteristics Initially there is severe pain in the temporal region, described as a throbbing headache associated with moderate fever leukocytosis general malaise prostration and sweats Pain may also be present in the scalp and eyes, which is precipitated by chewing coughing and sneezing

After several weeks of prodromal changes the skin over the superficial temporal artery becomes bright red and the vessel itself appears swollen prominent and tortuous These changes are apparent even at a distance from the patient Examination of the artery reveals a thickened vessel which is markedly tender Eventually pulsations may become absent Although the findings are generally limited to one

thoracic pressure due to straining at stool sudden exertion or intense physical effort Blunt force trauma to the chest by producing injury to a normal aorta, may also be responsible for the initiation of an aneurysm In the presence of a vessel weakened by disease this possibility is enhanced With regard to future developments in the lesion it is necessary to consider that as the blood circulates under pressure through an unclotted or fusiform aneurysm it creates a total strain on the sac wall which varies with the square root of the surface area[7] If the sac diameter doubles in size this force is increased by 100 per cent Therefore, a situation develops which is conducive to rupture since as the sac is stretched and the strength of its wall is correspondingly reduced the stress to which it is exposed is increased However in the presence of clot in the lumen the total effect of the force on the aneurysm is definitely diminished except at its mouth where conditions remain unchanged Another possibility is that if the aneurysm expands rapidly it may outstrip its blood supply, thus leading to anemic necrosis and rupture[9]

Clinical Course The symptoms of an intrathoracic aneurysm can for the most part be ascribed to pressure effects of the lesion Cough and dyspnea are common complaints being due to compression of the trachea or bronchi Voice changes consisting of hoarseness stridor or even complete loss of phonation generally result either from pressure on the recurrent laryngeal nerve associated with vocal cord paralysis or from narrowing of the trachea or bronchi Pain may be present due to pressure against the spinal column the sternum, or the anterior ends of the ribs It may vary in location and severity

The physical findings associated with an intrathoracic aneurysm consist of a pulsating mass in the infraclavicular fossae precordial pulsations signs of compression of the trachea and widening of the area of dullness at the base of the heart As a result of pressure on the trachea a tracheal tug or tracheal displacement may be present Considerable difference in blood pressure in the two arms and in the amplitude of the pulse at the wrist and in the neck may be noted However only rarely is there complete absence of pulsations in the radial ulnar or carotid artery on the involved side Various types of murmurs including to and fro or systolic bruits may be heard at the base of the heart or over the pulsating mass

The symptoms of an abdominal aneurysm may be variable and confusing In about one third of the cases there are no complaints referable to the lesion since it frequently grows insidiously The most common complaint is abdominal or low back pain which is poorly localized and defined and does not radiate Palpation generally reveals an expansile and pulsatile abdominal mass over which a thrill or bruit may be elicited The pulsations in the femoral arteries may be reduced but most often they are normal

Diagnostic Aids Fluoroscopy in various positions is frequently sufficient to identify localize and outline an intrathoracic aneurysm With the use of a barium swallow the degree of esophageal obstruction can be determined as well as the displacement by the mass Roentgeno-



Fig 65 Aortic aneurysms A Ruptured arteriosclerotic aneurysm of the abdominal aorta showing large mass of coagulated blood B Syphilitic aortic aneurysm of the ascending aorta showing thickness of wall of sac emptied of clot

Pathogenesis Although it is true that a healthy aorta is able to withstand any conceivable increase in blood pressure produced by a contracting ventricle a sudden high rise in pressure in a diseased vessel as during physical strain may cause rupture of the elastic fibers of the artery and a resulting dilatation This may take place in the presence of an intact adventitia Another factor which contributes to the formation of an aneurysm is a rise in intra abdominal or intra

the origin of the renal arteries information of great significance if surgical intervention is contemplated In fact if the results are clear-cut aortography may prevent a fruitless and dangerous exploratory operation

Differential Diagnosis The principal lesions which must be considered in the differential diagnosis of intrathoracic aneurysms are tumors located in the chest Distinguishing signs between the two can be elicited by means of the diagnostic aids already enumerated Bronchoscopy or esophagoscopy should never be attempted since there is always the possibility that either may contribute to rupture of the aneurysm Abdominal aneurysms may have to be differentiated from acute recurrent or chronic abdominal conditions The severe boring pain produced by the lesion may simulate the symptoms of renal colic perinephric abscess or hydronephrosis if it radiates along the ureters spermatic cord or round ligament

Treatment The treatment of intrathoracic and abdominal aneurysms of the aorta remains a very difficult problem Since there is no effective medical therapy most patients should be treated surgically especially in view of the very poor prognosis associated with nonintervention There is no age limit nor does hypertension predispose against such an approach Furthermore a cerebrovascular accident or a myocardial infarction is not a contraindication provided 4 to 6 months have elapsed since the acute phase However surgical procedures should not be used in the presence of myocardial failure renal failure or radiologic evidence of severe aortic calcification

Of the various measures utilized in the surgical treatment of aortic aneurysms, one consists of means to promote thrombosis and fibrotic organization of the contents of the sac This is attempted through ligation introduction of foreign material or stimulation of periarterial fibrosis Ligation is most effective if tape ligatures are tied around the proximal and distal portions of the sac and then the clot is evacuated With regard to the use of foreign materials the introduction into the lumen of the aneurysm of a silver wire over which a galvanic current is passed (wiring and electrothermic coagulation) appears to be best[5, 6, 8] This procedure produces a deposit of coagulated blood in the vicinity of the wire followed by propagation of the process throughout the sac Periarterial fibrosis is accomplished by the use of strips or sheets of reactive polythene-cellophane film in intimate contact with the aneurysmal sac[13] All structures in proximity to the lesion are first mobilized and separated from it so that they are not affected by the irritating substance

Other types of surgical therapy are obliterative restorative or reconstructive endoaneurysmorrhaphy and excision[11] However endoaneurysmorrhaphy can not be readily used in intrathoracic aneurysms of the aorta Extirpation of the sac preferably with restoration of normal blood flow is considered to be the procedure of choice by some workers[11] In this regard replacement of the diseased aortic bifurcation by a preserved aortic homograft can be accomplished in selected cases[13] It is clear that only in those instances in which the aneurysm is located below the origin of the renal arteries is this approach applicable It is possible that even thoracic aneurysms will in the future be treated by the use of homografts[13]

Before concluding the discussion of therapy it is necessary to point out that if

within the aneurysm However, it must be realized that in some instances no pulsations will be demonstrated while solid nonvascular tumors may, on occasion, show transmitted pulsations from the heart or great vessels If there is any doubt as to the continuity of the mass with the aortic arch oblique tomograms may be taken to demonstrate this connection Angiocardiography may also be of value Penetrating films of the sternum ribs, and spine are useful since they may show signs of bone erosion, a fairly common finding in intrathoracic aneurysms Aside from roentgenologic aids, blood Kahn and Wassermann tests are frequently positive in the presence of intrathoracic aneurysms



Fig 64 X ray of syphilitic aneurysm of ascending aorta showing calcification of sac A Posteroanterior view B Lateral view

In the case of an abdominal aneurysm, a number of laboratory diagnostic aids are available A scout roentgenogram is an excellent means of outlining the sac, provided it contains scattered calcified plaques or curvilinear or laminated calcification Even the presence of a large soft tissue mass may be visualized in this manner Erosion of the vertebral bodies is an infrequent finding in the case of the arteriosclerotic aneurysm of the lower segment of the abdominal aorta but is much more common in the presence of syphilitic involvement of the upper portion Retrograde pyelograms may demonstrate displacement of the ureters from their normal position

Recently aortography (Chap XXV) has been used to determine the shape of the aneurysm the size of its neck and the width of the laminated clot The procedure is also of use in ascertaining whether the lesion arises above or below

the origin of the renal arteries information of great significance if surgical intervention is contemplated. In fact if the results are clear-cut aortography may prevent a fruitless and dangerous exploratory operation

Differential Diagnosis The principal lesions which must be considered in the differential diagnosis of intrathoracic aneurysms are tumors located in the chest Distinguishing signs between the two can be elicited by means of the diagnostic aids already enumerated. Bronchoscopy or esophagoscopy should never be attempted since there is always the possibility that either may contribute to rupture of the aneurysm Abdominal aneurysms may have to be differentiated from acute recurrent, or chronic abdominal conditions The severe boring pain produced by the lesion may simulate the symptoms of renal colic, perinephric abscess or hydronephrosis if it radiates along the ureters spermatic cord or round ligament

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Before concluding the discussion of therapy it is necessary to point out that if

an abdominal aneurysm is ligated, there is always the risk of serious impairment of blood flow to the lower extremities, since the stimulation for the formation of an efficient collateral circulation does not exist in the presence of such a lesion Furthermore, there is some evidence to indicate that aside from possibly the use of homografts, the other procedures do not appear to increase materially the life span of patients with aortic aneurysms

Prognosis Aneurysms of the thoracic and abdominal aorta have a grave prognosis, since in most instances the condition is progressive and ultimately fatal Analysis of a large series of cases of thoracic aneurysms has shown that the average duration of life after the onset of symptoms is from 6 to 8 months [3] Regarding abdominal aneurysms, the life expectancy curve indicates that the survival rate is much lower than that of the normal population,[1] the prognosis being poorer for the syphilitic than for the arteriosclerotic lesion

Complications and Sequelae The most serious complication of aortic aneurysm is rupture of the sac with loss of blood into the thoracic or abdominal cavity (Fig 63A) This is almost invariably associated with a state of shock, unless the leak is small and quickly sealed off It is of interest that the process takes the form of a direct through and through rupture rather than a burrowing or longitudinal dissection in the aortic wall [1]

In abdominal aneurysm the extravasation of blood is generally found in the retroperitoneal space, while massive rupture into the peritoneal cavity occurs only rarely However, small amounts of free fluid sometimes bloodstained, may be found in the peritoneal cavity

The symptoms and signs of lower aortic rupture are fairly typical Pain is sudden and very severe being described as agonizing tearing and piercing [1] It is most often localized to the lower abdomen or lower back There is also marked pallor of the face even greater than that associated with shock Another common physical finding is tenderness in the abdomen at the site of the aneurysm, and in the loin, *representing the pathways produced by the extravasated blood* Generally, there is also an exquisitely tender palpable abdominal mass at the aneurysmal site Pulsations in the femoral arteries may or may not be reduced X ray examinations may reveal a rounded soft tissue shadow or a loss of psoas outline

Of lesser significance are the sequelae which result from pressure of the expanding vascular tumor on the neighboring structures Compression of peripheral nerves by an abdominal aneurysm may produce neuritis and even paralysis in the lower extremities Findings simulating acute deep thrombophlebitis may likewise be present, due to pressure of the vascular tumor on the iliofemoral vein and associated lymphatics These may consist of marked swelling of the foot, leg and even thigh and tenderness in the deep femoral triangle Venograms are generally of little use in differentiating the aneurysm from a deep thrombophlebitis

DISSECTING AORTIC ANEURYSM

Dissecting aneurysm is a vascular condition in which a tear in the aorta occurs followed by separation of the layers of the media of the vessel both proximally

and distally It is found much more frequently in men than in women between the ages of 50 and 70 years Hypertension is present in more than half the cases The disease may also be observed in individuals below the age of 40 years but under such circumstances there is usually an associated coarctation or hypoplasia of the aorta

Pathology and Pathogenesis The lesion generally begins with cystic degeneration of the media of the aorta (*cystic medial necrosis of Erdheim*[16]) which results in patches of muscle necrosis or cysts filled with mucoid material These changes are followed by rupture of the nutrient medial vessels causing a hematoma which splits the medial layers and breaks through the intima The entry of blood from the lumen of the aorta further enlarges the sac The dissection usually starts between the heart and the aortic arch and may progress either distally *or proximally to the aortic ring If death* does not occur with the initial rupture the aneurysm *may convert the aorta to a double* barrelled tube As dissection takes place the various arteries arising from the vessel at the site of involvement are either occluded or destroyed The most frequent sites of predilection for *dissecting* aneurysm are the first part of the ascending aorta and the beginning of the descending aorta locations which also are vulnerable *to traumatic arterial* aneurysms

Clinical Characteristics The symptoms and signs of dissecting aneurysm are *protean* the type depending upon what portion of the aorta is involved Clinically the *findings* can be divided into five different patterns pulmonary *cerebral cardiovascular* renal and gastrointestinal *In most instances the initial tear is associated with a state of shock* which *may or may not be fatal A sudden ripping* pain in the chest or epigastrium is usually *experienced with spread to the* shoulder back abdomen kidneys or groin

If dissection *takes place* in the direction of the heart the orifices of coronary vessels *may be affected* producing symptoms similar to myocardial infarction Aortic diastolic *murmurs may* be heard and generally *there is a tachycardia* Rupture may also occur into the pericardial sac *to cause cardiac tamponade* or into the pleural cavity resulting in collapse of the lung *and painless* dyspnea

If dissection is downward into the *abdominal aorta* the symptoms are primarily gastrointestinal in type Constant epigastric *pain may* be present with physical findings simulating large bowel obstruction *or other types* of surgical emergencies There may even be evacuations *of large quantities* of free blood Neurologic findings are frequent and at times bizarre *If the spinal arteries* are involved in the dissection there may be complete *paralysis of the lower* extremities In those instances in which the aneurysm has *extended down* to the bifurcation of the aorta the pulsations in the femoral *arteries are* generally reduced or absent These changes may also be attributed in *part to the* existing state of shock

Diagnosis Until recently a *dissecting* aneurysm was rarely diagnosed ante mortem but with a greater amount of *attention* now being paid to this entity it is almost routinely considered in *the differentiation* of unusual symptom complexes involving the chest or *abdomen* Of value in diagnosis is the use of serial roentgenograms which may demonstrate a slowly or rapidly enlarging aortic or supracardiac deformity[2] The electrocardiogram *may show* signs of nonspecific

myocardial involvement, of pericarditis, or even of myocardial infarction. Examination of the blood and urine may indicate the presence of renal impairment. Leukocytosis is common and progressive anemia may be noted.

Therapy. The treatment of dissecting aneurysm is, for the most part, symptomatic. There appears to be little advantage to surgical intervention, although this approach has been inadvertently utilized in instances of an incorrect diagnosis of an acute abdominal emergency. Because of the generally widespread involvement of the wall of the aorta by the process, attempts to repair the vessel are unsuccessful.

Prognosis. The prognosis of dissecting aneurysm is very grave, although at times the patient may recover from the initial state of shock. However, this is generally followed by further extension and eventually rupture of the aneurysm and death. If dissection produces obliteration of such vital vessels as the renal arteries, uremia occurs.

MESENTERIC VASCULAR OCCLUSION

By mesenteric vascular occlusion is meant complete obstruction of either the superior or inferior mesenteric artery or the corresponding vein, producing an anemic infarct and hemorrhagic necrosis of loops of small intestine.[30] As in the case of sudden arterial occlusion in the extremities, the condition can be considered a real surgical emergency. It is found most often in patients between the ages of 30 and 65 years and rarely in children. The incidence is much greater in males than in females.

Etiology. In the case of involvement of either mesenteric artery, the etiologic factor has generally been considered to be an embolus rather than a thrombus, although this view is not consistently supported by case reports.[1] The incidence of closure of the superior mesenteric artery by an embolus is much greater than that of the inferior mesenteric artery.

Occlusion of the superior or inferior mesenteric vein is due almost invariably to thrombosis (Fig. 65). It is generally associated with involvement of abdominal organs, as for example appendicitis, diverticulitis, ulcerative colitis, pelvic inflammatory disease, carcinoma, and strangulated bowel.[19] Also implicated as precursors of this condition are trauma to mesenteric veins, mechanical causes (portal stasis, adhesions and bands, and pressure from tumors), and diseases which predispose to thrombus formation, such as polycythemia and sickle cell anemia. In a small group of patients no cause may be uncovered.[4]

Clinical Characteristics. The clinical picture of mesenteric vascular occlusion may vary considerably depending upon several factors. Among these are the location and size of the occluded vessel and the degree of collateral circulation. Obstruction just proximal to the terminal arcade will rarely cause gangrene of the bowel, unless very large vessels are involved.[4] It is also of interest in this regard that the lower half of the large bowel has a much better collateral circulation than the upper half or the small bowel.[1] Another factor which will influence the clinical picture is the rapidity of the process. Sudden occlusion will produce char

acteristic signs and symptoms, while in the case of slow obstruction there may not be any obvious clinical changes

As in the case of pulmonary infarction the previous state of the intestinal circulation may also affect the severity of the condition Congestive heart failure chronic pulmonary disease and stasis due to portal hypertension may produce hypervolemia and polycythemia with resulting engorgement of the vessels and a reduction of the distensibility of the collateral bed[31] As a consequence the pathologic alterations produced by obstruction of the main vessel will be exaggerated

The typical clinical story of mesenteric vascular occlusion begins with a sudden



FIG 6, Mesenteric vein thrombosis with gangrene of intestinal loops

onset of generalized knifelike abdominal pain not easily controlled by opiates and in most instances colicky in type Vomiting is frequently present from the onset Profound shock is noted in about half the cases of arterial mesenteric occlusion but is a rare and late sign of venous occlusion[4] When intestinal obstruction occurs all the findings are aggravated if diarrhea existed before it now ceases Distension of the abdomen and fluid loss into the peritoneal cavity and intestine are greater in venous occlusion than in the arterial form

With the onset of intestinal strangulation an abdominal mass may be felt associated with hematemesis and melena Rectal examination often reveals blood on the examining finger The temperature may be subnormal or slightly elevated while there may be a moderate or very high leukocytosis (between -5 000 and 40 000 with 85 to 9, per cent polymorphonuclear leukocytes)

Treatment and Prognosis If the diagnosis is made soon enough the procedure

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Treatment and Prognosis If the diagnosis is made soon enough the procedure

of choice in mesenteric vascular occlusion is resection of the gangrenous loop and end to-end or side to side anastomosis Despite the possible risk of hemorrhage in the operative wound, anticoagulants, in the form of the combined use of heparin and dicumarol, should be instituted promptly after operation Unfortunately, in most instances, surgical intervention is delayed too long and then such an approach is of no value in saving the patient s life If operation is not performed however, the mortality rate with superior mesenteric artery occlusion is 100 per cent [68] It is possible that thrombosis of the superior mesenteric vein is associated with a slightly better prognosis

PULMONARY ARTERIOVENOUS FISTULA

Pulmonary arteriovenous fistula has only recently received sufficient clinical attention to permit an antemortem diagnosis It is found primarily in males, between the ages of 17 and 30 years, and is probably congenital in origin The condition has not been considered a disease entity in itself but instead has been defined as a part of a vascular defect presenting a varied pattern depending upon the extent and location of associated vascular lesions Characteristically there are also present multiple telangiectatic lesions of the mucous membranes, the gastro intestinal tract and the skin of the face neck and lips (See *Hereditary hemorrhagic telangiectasia* Chap XXIII)

Pathology and Pathogenesis The aneurysm consists of a lobulated thin walled branching pulsating pulmonary sac of varying size, made up of both an arterial and a venous component [3] This structure produces a shunt in the lung whereby *a considerable amount of blood passes from the arterial to the venous* portions of the pulmonary circuit without traversing the capillaries of the alveoli As a consequence the oxygen saturation of the arterial blood in the systemic circulation falls, the degree of unsaturation depending upon the effective size of the *arteriovenous communication*

Clinical Characteristics As a result of the low oxygen saturation of the blood the patient generally manifests cyanosis of the face hands, and feet and clubbing of the fingers and toes However it is necessary to point out that in some in*stances a well developed pulmonary arteriovenous aneurysm may* exist in the absence of these signs the explanation for this discrepancy is not clear Other common findings consist of bleeding from the nose and a continuous loud harsh bruit heard over the site of the tumor which is synchronous with systole of the heart and is accentuated by deep inspirations *Despite the fact that many* of the patients complain of exertional dyspnea, no abnormalities are noted in the heart, the electrocardiogram or the blood pressure The spleen is not enlarged and bone marrow studies are normal

Diagnostic Aids Of greatest value in making the diagnosis of pulmonary arteriovenous fistula is the roentgen examination A mass is generally demonstrated either as a saccular cirsoid, or racemose cluster of sharply defined structures with uniform density, or as enlarged branching tributary vascular channels [6] Although these findings can be visualized using standard technics they are better demon

strated by laminography which permits differentiation of the arterial and venous trunks[28] Angiography is of value in outlining the vessels comprising the mass and in determining whether or not multiple aneurysms exist Such information is helpful in the subsequent surgical treatment of the condition The Valsalva maneuver may be useful in demonstrating the vascular nature of the mass With an increase in intrathoracic pressure produced by the test there may be a reduction in its size as observed by x ray or fluoroscopy

Studies on the blood are also essential in the diagnosis of the disorder In most instances the peripheral blood shows an increase in erythrocyte count hematocrit and hemoglobin with an elevated total blood volume but little or no change in plasma volume Studies of arterial blood almost invariably reveal a reduction in oxygen saturation

Differential Diagnosis Among the several conditions characterized by cyanosis which must be differentiated from pulmonary arteriovenous fistula is polycythemia vera However this disorder is found in an older age group and is characterized by the presence of splenomegaly with abnormalities of blood and bone marrow morphology [9] The possibility of secondary polycythemia can also be eliminated because of the absence of any factors producing it such as chronic pulmonary disorders exposure to high altitude or poisoning by heavy metals or aniline dyes Congenital heart disease can be ruled out by roentgenographic electrocardiographic and physical findings In pulmonary arteriovenous aneurysm the cyanosis is generally of later development the heart size and contour are normal and cardiac murmurs are usually absent At the same time roentgen evidence of vascular tumors is present in this condition and not noted in congenital heart disease

Treatment In view of the resulting complications of polycythemia and the possibility of a lethal hemoptysis and fatal hemothorax from a pulmonary arteriovenous fistula it is the opinion of most workers that such a lesion should be surgically removed This should be carried out even in the absence of symptoms cyanosis or polycythemic changes [8] However if there are several aneurysms in different lobes the difficulties of surgical extirpation are increased The type of approach depends upon the size of the lesion and varies from simple ligature of the involved arteries and veins to total pneumonectomy [8]

SUPERIOR VENA CAVA SYNDROME

Obstruction of the superior vena cava may result from a number of unrelated conditions Chronic mediastinitis due to tuberculosis syphilis or other chronic disorders may produce the syndrome by involvement of the vessel in the process while a similar response may follow pressure from primary malignant tumors of the bronchus from lung or mediastinal lymph nodes from a metastatic carcinoma of the breast and from an aortic aneurysm Local inflammation of the superior vena cava may also cause complete obliteration of the vessel Thrombosis is usually associated with mediastinal infection or trauma or it may occur with congestive heart failure Occasionally it may happen spontaneously It can likewise

develop with any of the conditions which compress or invade the superior vena cava

Clinical Characteristics Common complaints of the patient suffering from obstruction of the superior vena cava are headache, dizziness and a feeling of fullness in the head, probably due to the increase in venous pressure in the cerebral vessels

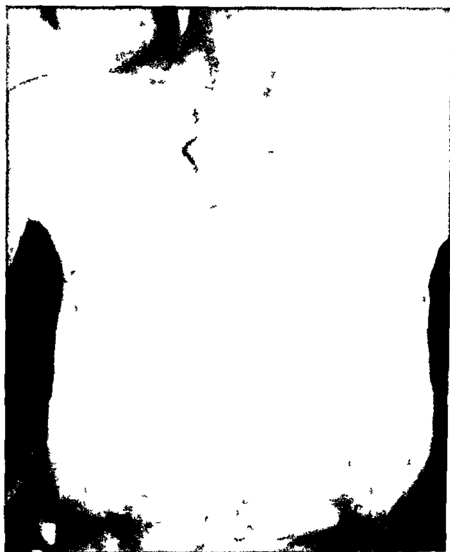


FIG 66 Marked collateral venous network on the anterior portion of chest and abdomen produced by complete obstruction of the superior vena cava Network made more apparent by the use of infrared photography

from obstruction to venous inflow to the heart At the same time various types of respiratory difficulties such as dyspnea orthopnea and periodic breathing may be present These changes have been attributed to slowed cerebral blood flow and a resulting venous stasis in the respiratory center [1] The common symptoms of tightness around the tracheal cartilages and a choking sensation may be due to pressure of the distended veins in the neck on the neighboring structures All these com

plaints are aggravated when the patient bends over to tie his shoes get into a bath or pick up something from the floor As the condition progresses even very mild effort will elicit the symptoms

The findings of obstruction of the superior vena cava are quite characteristic and hence the diagnosis of this condition should offer little difficulty Among the earliest signs are numerous small isolated purple venules distributed over the chest wall and puffiness and swelling of the eyelids Later striking venous engorgement and edema of the neck head and arms appear together with dilated superficial veins on the chest and abdomen (Fig 66) [9] In the recumbent position the neck veins assume a cordlike appearance and the face becomes suffused with blood

Several tests can be performed which help considerably in arriving at the proper diagnosis An important finding is the marked increase in collateral circulation made more apparent either by having the patient perform the Valsalva maneuver or by making use of infrared photography (Fig 66) Venography will allow visualization of the superficial vessels and at the same time may localize the site of obstruction If the occlusion is complete the usual outlining of the cardiac chambers and great vessels will not take place A confirmatory test is *venous pressure* measurements obtained in the upper and lower extremities An elevated reading from the veins at the cubital fossa and a normal one from the femoral vein support the diagnosis of obstruction of the superior vena cava

The response to the application of a tight tourniquet around the lower portion of the chest may be of value in localizing the site of obstruction in the superior vena cava If the occlusion is below the level of entry of the azygos vein such a measure will cause a prompt and marked rise in venous pressure in the arm due to compression of the superficial collateral veins carrying blood from the upper part of the body to the right atrium via the inferior vena cava [3] With the obstruction above the level of entry of the azygos vein no rise in venous pressure will occur since under such circumstances blood is entering the heart through the azygos vein and the portion of the superior vena cava proximal to the occlusion (For discussion of collateral venous networks present in the superior vena cava syndrome see *Collateral venous networks resulting from obstruction of specific vessels* Chap XXVI)

Differential Diagnosis Since inferior vena caval obstruction is also followed by the production of an extensive superficial venous collateral system it is necessary to differentiate this condition from superior vena caval obstruction Of importance is the direction of movement of blood in the collateral vessels with the patient lying supine This is determined by picking out two dilated veins on the anterior abdominal wall one located above and the other below the umbilicus and milking each one free of blood by spreading two fingers along the course of the vessel On removal of first one and then the other finger the direction of filling can be determined In superior vena caval obstruction both veins should fill from above while the reverse is true for inferior vena caval obstruction Of further value in distinguishing the two conditions is the difference in the venous pressure measurements obtained in the upper as compared with the lower extremities

develop with any of the conditions which compress or invade the superior vena cava

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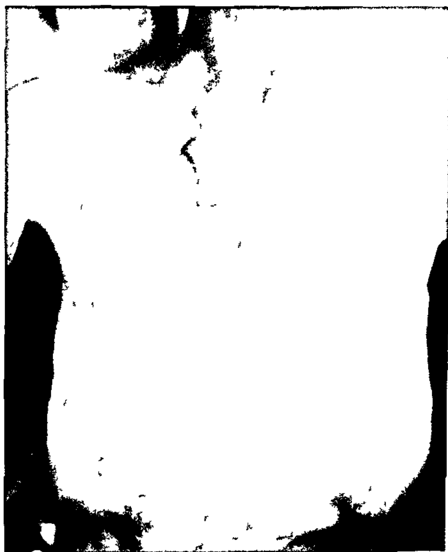


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Treatment The treatment of superior vena caval obstruction depends upon the underlying pathology In the case of mediastinal lymphoma, irradiation, nitrogen mustard, ACTH or cortisone may be worthy of clinical trial [0] *When a* chronic fibrous mediastinitis is the causal agent, mediastinotomy with lysis of adhesions has been recommended Phlebotomy may give symptomatic relief to *some patients*

Prognosis It is generally accepted that when the etiologic factor is benign, venous hypertension resulting from obstruction of the superior vena cava does *not necessarily affect longevity In* other instances, the prognosis will depend upon the type of malignant tumor causing the obstruction

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ION TRANSFER (IONTOPHORESIS)

As has already been indicated the local administration of a drug through ion transfer has definite value since the therapeutic effect is limited to the area under treatment while systemic responses are ordinarily minimal By ion transfer is meant the use of a low density galvanic electric current to introduce and deposit a medication into the deeper layers of the skin from which depot the substance can be gradually absorbed to exert its pharmacologic action on the local vessels

Technic The ordinary type of galvanic machine is utilized The negative pole is attached to a large plate electrode which is held firmly against the anterior abdominal wall or the back while the positive pole is connected either to a long strip of pliable metal about 45 cm long and 4 cm wide (18 inches long and 1½ inches wide) or to a regular type electrode which is suspended in a bakelite basin If the former is utilized the involved limb is covered with gauze soaked in a solution of the desired drug followed by sheets of asbestos paper also saturated with the medication The strip electrode is then spiraled around the limb and held tightly in place by an ordinary roller bandage care is taken to prevent the metal from touching any portion of the skin not covered by asbestos If an open ulcer is being treated it may be advisable to cover it with a piece of rubber sheeting before applying the gauze in order to minimize the possibility of local concentration of the current producing further destruction of tissues

[illegible] e nonconductor ba[illegible] A simple type of [illegible] is suspended in the medication by attaching it to the wall of the container and the limb is inserted as far away from the electrode as possible

The treatment is begun using approximately 5 ma of current and rapidly working it up in steps to *15–30 ma* The procedure is continued at this level for 45 minute or more and then the current is quickly reduced to zero With the use of the spiral wire at times there may be a little prickling sensation beneath the electrodes during the treatment but this can generally be eliminated by making firmer contact with the surface of the body

Clinical Application Ion transfer of vasodilating agents has been proposed as therapy in several peripheral vascular disorders For example Mecholyl (acetyl β methylcholine chloride) in 0 1–0 5% *solution* has been used in the control of ulceration present with venous stasis and in the treatment of sclerodermatous changes in the hands Histamine in a 1 10 000 aqueous concentration has had similar clinical application Formaldehyde in a 1% solution is of value in counteracting hyperhidrosis associated with *vasospasm* in such conditions as the post-trench foot syndrome and posttraumatic vasomotor disorders The current density used is 10–1[illegible] ma which is less than with the other two drugs (15–30 ma)

Untoward Effects The one serious complication of ion transfer is the production of a burn where *the metal* electrode has come in direct contact with skin Such a lesion is frequently unresponsive to treatment and hence every precaution should be taken to prevent its formation With regard to side reactions from the

CHAPTER

XXV TECHNICS OR THERAPEUTIC MEASURES REQUIRING SPECIAL EQUIPMENT OR SKILL

There are a number of diagnostic and therapeutic procedures which are of use in peripheral vascular disorders but which can not be performed by the physician in his office or in the patient's home because of the need for special equipment and/or trained technical assistance For this reason such material has not been discussed in the running contents of the book, and instead has been placed in the present chapter, where it does not interfere with the continuity of the text and still is available if the occasion arises for its clinical application Not included are primarily surgical technics and methods used in the anesthetization of paraverte bral sympathetic ganglia since adequate descriptions of such measures are found in monographs on these subjects[6 7 8]

INFRARED PHOTOGRAPHY

Infrared photography may prove of value in obtaining information regarding the scope and ramification of a superficial collateral venous network This procedure involves the use of film which is especially sensitized to respond to infrared rays and filters which pass the invisible infrared band only excluding the shorter wave lengths (both visible and invisible) of the rest of the spectrum An infrared pho tograph can *thus outline the superficial veins by virtue of the hemoglobin con* tent of the blood circulating through them (Figs 35 p 260 and 67)

Technic Infrared film is used together with special filters generally of the Wratton type No 25 No 89 or No 87 The latter filter transmits the longest wavelength and is the most efficient for medical photography An ordinary camera can be utilized and if the photograph is taken in artificial light two No 2 photo flood lamps in proper reflectors will supply sufficient illumination since they are rich in infrared radiation Under these circumstances the exposure will have to be lengthy (1 second at f/8 with the source of light 3 feet from the subject using a No 87 filter) The infrared film should be handled and developed in total dark ness or with the use of an infrared Safelight Having the patient stand up when he is being photographed produces better visualization of the veins since gravity tends to distend them with blood

ARTERIOGRAPHY

One means of studying the ramifications of the arterial system is through the use of radiopaque substances Various contrast media have been proposed for

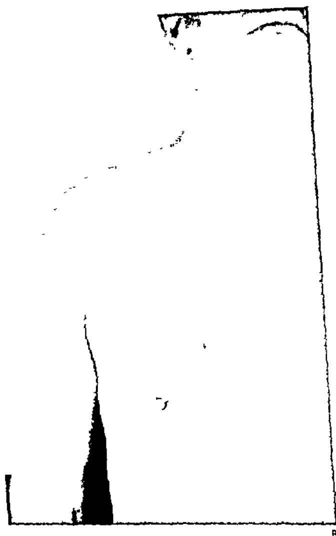


FIG 67 (*Continued*) B Photograph of same patient using ordinary technic and film

this purpose but the one most widely advocated is Diodrast a complex iodine compound An apparatus which permits rapid changing of films is a very helpful adjunct to the x ray equipment since it allows for repeated exposures in quick succession The single film method although requiring no special equipment, seldom gives as much information

drugs themselves, Mecholyl by ion transfer is generally associated with none, since choline esterase in the tissues rapidly destroys any quantity of the material which has penetrated below the skin However, on occasion sweating flushing salivation, hypotension, and increased intestinal peristalsis may occur during the procedure



FIG 67 A Visualization of superficial venous channels in a patient with axillary vein thrombosis using infrared photography

Hence it is advisable to have a syringe containing atropine sulfate 0 65 mg (1/100 gr) available in order to terminate the action of Mecholyl

In the use of formaldehyde by ion transfer a dermatitis may at times develop because of sensitivity of the skin to this agent It is therefore necessary to skin test all patients before using the medication

At the end of this time, a single 4 second x ray exposure is made during which period the limb is firmly immobilized to prevent blurring This prolonged exposure permits wide distribution of the contrast medium in the arterial tree

Translumbar Arteriography (Aortography) Recently the technic of direct injection of contrast medium into the abdominal aorta has received considerable attention Although it has been utilized primarily to outline the vascular tree in the

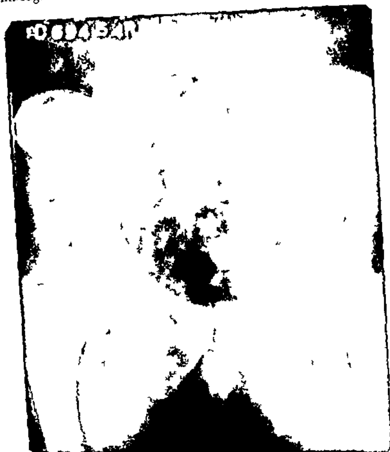


FIG. 68 (*Continued*) B Case of arteriosclerosis obliterans showing absence of deep femoral artery on the right side

kidneys and other abdominal organs it is also of value in the visualization of aneurysms and obstructions of the abdominal aorta and iliofemoral arteries (Fig 68)

The patient is placed on the x ray table and if necessary anesthetized with intravenous sodium pentothal (Thiopental) The back is prepared surgically and then a #18 gauge needle about 15 cm (6 inches) long is inserted 8 cm (3 2 inches) to the left of the spinous processes at the lower edge of the twelfth rib[10, 11] The needle is first directed upward and medially toward the twelfth vertebral body withdrawn somewhat, and then reinserted several times changing the direction

Technic

Visualization of Vessels of Extremities In the case of the upper limb, 15–30 cc of 35 or 70% contrast medium is injected percutaneously into the brachial artery above the elbow over a period of 2–3 seconds, and then the first film is exposed The subsequent exposures are made as rapidly as possible (one or two per second),



FIG 68 Translumbar arteriography A Case of arteriosclerosis obliterans showing occlusion of the main branches of the left common iliac artery as well as main branches in both lower extremities

with the film and x ray beam centered over the area under study A similar procedure is utilized for the lower extremity where the injection is made into the femoral artery in the groin

If a rapid film-changer is not available an alternate method can be used This consists of injecting 50 cc of 35 or 70% contrast medium through a long piece of rubber tubing* attached to the needle in the artery over a period of 5–8 seconds

* With this procedure the member of the team performing the injection does not have to wear protective gloves since he can stand some distance away from the x ray tube As a result he is able to carry out his task more efficiently

At the end of this time a single 4 second x ray exposure is made during which period the limb is firmly immobilized to prevent blurring This prolonged exposure permits wide distribution of the contrast medium in the arterial tree

Translumbar Arteriography (Aortography) Recently the technic of direct injection of contrast medium into the abdominal aorta has received considerable attention Although it has been utilized primarily to outline the vascular tree in the



B

Fig 68 (*Continued*) B Case of arteriosclerosis obliterans showing absence of deep femoral artery on the right side

kidneys and other abdominal organs it is also of value in the visualization of aneurysms and obstructions of the abdominal aorta and iliofemoral arteries (Fig 68)

The patient is placed on the x ray table and if necessary anesthetized with intravenous sodium pentothal (Thiopental) The back is prepared surgically and then a #18 gauge needle about 15 cm (6 inches) long is inserted 8 cm (3 2 inches) to the left of the spinous processes at the lower edge of the twelfth rib [10, 11] The needle is first directed upward and medially toward the twelfth vertebral body withdrawn somewhat, and then reinserted several times changing the direction

slightly with each trial, until the point is felt to slide off the body of the vertebra into the aorta If the attempt is successful, oxygenated blood will well out of the needle on removal of the stylet A Sani Lok control syringe with a metal plunger, filled with 12 cc of 75% contrast medium, is connected to the needle and the full amount is rapidly injected into the vessel (1–2 seconds), provided there is free retrograde blood flow into the syringe The x ray film is exposed for 0 2 second after a delay of up to 6 seconds following completion of the injection to permit the medium to reach the area to be studied For visualization of the iliofemoral artery, the contrast medium may be given at a lower level in the aorta

Contraindications and Untoward Effects Arteriography is not without danger to the patient It should probably not be used in individuals with a history of iodide allergy, hyperthyroidism or severe kidney and liver damage Because of reported fatalities due to hypersensitivity to the contrast medium in every case the injection should be preceded by the intravenous administration of a very small quantity of the material as a test dose At the same time it is essential to have epinephrine 1 1000 available for intravenous injection should symptoms develop Other side reactions include an erythematous eruption wheals, nausea, vomiting cyanosis and a fall in blood pressure but these reactions are uncommon and generally last only a short time

Several different untoward effects may occur in the extremities following the injection Among these are the formation of a hematoma and extravasation of the contrast material into the tissues The latter response may produce an inflammatory reaction unless moist heat is applied to encourage resorption Not infrequently pain is experienced during the arterial injection probably because of spasm As the contrast substance fills the arterial tree, the patient may experience a feeling of warmth and a severe sharp pain that spreads down the extremity Occasionally this is followed by various types of vasomotor disturbances and rarely, vasoconstriction of such a degree as to produce actual occlusion of a main artery, followed by gangrene

There have been few serious complications reported in translumbar arteriography despite the blind approach to the aorta Extravascular injection into the soft tissues is not uncommon but it causes minimal symptoms Recognizable hematoma of significant proportions has not been encountered Rarely intraperitoneal insertion of the needle has occurred with subsequent signs of peritoneal irritation, and several instances of permanent paraplegia have been noted Direct injection of the contrast medium into one of the major visceral arteries is not rare but with the organic iodides now in use, this has generally not resulted in serious sequelae

Clinical Application Arteriography is of value in obtaining information concerning the caliber of the lumen and the contour of the inner wall of large arteries and hence in determining whether partial or complete obstruction exists At the same time, it affords an opportunity for the study of the extent of collateral circulation It may also be useful in differentiating arteriosclerosis obliterans from thromboangiitis obliterans (p 137) Recently it has been found helpful in the localization of sites of segmental obstruction of arteries (Fig 16A p 158) preliminary to thromboendarterectomy or surgical removal of the occluded portion

and substitution of a venous or arterial graft The procedure can be used in outlining the ramifications of congenital and acquired arteriovenous fistulas in differentiating them from arterial aneurysms (Fig 41 p 398), and in determining whether or not their surgical repair has been successful It is likewise of aid in localizing such lesions when this is not possible by the usual clinical procedures

Precautions in Interpretation of Results At times injection of the contrast medium produces arterial spasm particularly in the case of patients with Raynaud s disease or Raynaud s syndrome in whom the vessels are ordinarily unduly sensitive to noxious stimuli This response may prevent the material from entering some of the patent vessels with the result that they will not be visualized on the roentgenogram Such a response may lead to the erroneous conclusion that the unfilled vessels are occluded However the artifact can generally be recognized by the fact that the shadow of the lumen of the vessel ends in a point while in the presence of structural disease there is a tendency for a more blunt termination, with the portion of the lumen proximal to the obstruction showing increasing irregularity

VENOGRAPHY

The procedure of roentgenographic visualization of the venous tree of the extremities through the use of radiopaque material is in general similar to that utilized in arteriography Again the strength of the contrast medium most often employed is 35 or 70%

Technic A number of different methods have been proposed for study of the deep venous system of the lower extremity One consists of cannulating a constant small superficial vein present behind the lateral malleolus which communicates with the deep veins[4] The patient lies on a Bucky table with the limb under study extended moderately abducted and the foot everted Under local anesthesia, a vertical incision 1 5 cm (approximately ½ inch) in length is made about 1 cm (½ inch) posterior to the lateral malleolus at the site of the vein mentioned above This vessel is exposed sufficiently to permit insertion of a #19 transfusion cannula Then 20 cc of 35 or 70% of the contrast medium is injected over a period of 60 seconds immediately after which an x ray exposure of the leg is made The next steps in order consist of washing out the vein with physiologic saline removing the cannula tying the vessel and closing the skin with silk If a #19 needle is used instead of the cannula it is generally not necessary to ligate the vein

A procedure that obviates the need of exposing the vein surgically consists of percutaneous insertion of a # 1 needle into a subcutaneous vein on the dorsum of the foot or lateral side of the ankle with the patient s legs in dependency[6] The needle is strapped in place with adhesive and connected with an infusion set containing isotonic saline which is permitted to drip rapidly into the vessel so as to prevent clotting The patient is then placed on the x ray table with the casette containing the film behind the calf and thigh A rubber tourniquet is applied around the leg at the junction of the middle and lower third with sufficient pres

sure to prevent the contrast medium from entering the superficial veins of the upper part of the leg and thigh The remaining steps are similar to those described for the previous method

Recently a modification has been proposed which is useful in deriving information regarding the competency of the valves in the deep veins[3] A venogram is obtained in the usual manner and then, with 10 cc of the contrast medium still in the syringe the patient performs a Valsalva maneuver by closing his lips, holding his nose, and expiring forcibly While this step is being carried out the rest of the radiopaque material is injected into the vein The effect of increasing the intra abdominal pressure by the Valsalva maneuver is to reverse the direction of the column of contrast medium in the veins of the limbs As a consequence, closure of the valve cusps and bulging of the paravalvular sinuses occur, changes which are apparent in the venogram In the presence of incompetent valves, the Valsalva maneuver does not bring out such a response

Another method of outlining the deep venous system in the lower extremities is retrograde venography[9] The patient is placed supine on an x ray table with attached foot rest and the tube is tilted 60 degrees with the feet down An 18 by 43 cm (7 by 17 inch) film is placed under the thigh and lower portion of the pelvis and a second film of the same size under the leg The femoral vein is entered just below the inguinal ligament, using a #18 needle, and 30 cc of 35% of the contrast medium is injected slowly Two exposures are made immediately after the completion of the injection, and while the films are being removed and replaced by others, the patient exercises vigorously by raising himself on his toes ten times Then a second pair of exposures is made one minute after termination of the physical effort Clearing of the veins of contrast medium following exercise helps support the view that the valves are competent

Visualization of the deep venous system in the upper extremity requires a much less complex technic Since the block is generally located in the proximal portion, it is necessary to inject only 10 cc of 35% of contrast medium into the median cubital vein at the elbow to outline the large venous channels of the arm and the axillary vein

Untoward Effects As in arteriography, venography may be associated with serious side reactions due to the parenteral administration of the contrast medium The contraindications are similar for the two types of procedures With venography there is the added risk of either initiating or increasing venous thrombosis

Clinical Application Although when first presented venography won many advocates recently there has been a swing away from its routine use In the acute phase of thrombosis of the small deep veins of the calf and foot the findings should be interpreted with caution especially since the absence of contrast material in such vessels is not unequivocal evidence for the existence of occlusion In fact, false interpretations may be obtained in approximately one third of the patients with this disorder

Errors in which the contrast medium fails to enter the patent vessels may be due either to technical difficulties or to spasm of veins caused by the injection Spasm manifests itself by almost complete obliteration of a portion of the vessel with tapering distally and proximally and segments of normal caliber on either

side At times difficulty is encountered differentiating this appearance from that which follows structural alterations

When it is necessary to establish whether or not a patient has had an old deep thrombophlebitis venography is of considerable value It may bring out a filling defect in the main venous channel with collateral vessels bridging the gap or the vein may not be visualized at all being replaced by a weblike mass of smaller venous collaterals both deep and superficial In conjunction with the Valsalva maneuver venography is also helpful in determining valvular incompetency in the deep veins It is especially important if ligation of varicosities is contemplated in an individual with an equivocal history of deep thrombophlebitis

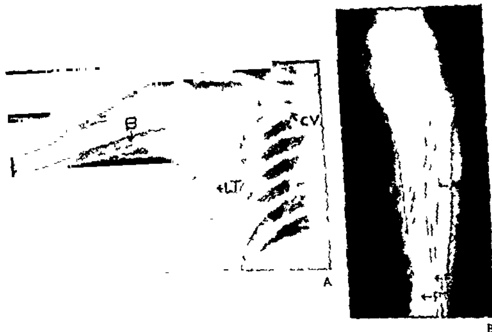


FIG 69 Occlusions of venous system visualized by venography A Block in basilic vein (B) (CV) subpectoral collateral veins (LT) lateral thoracic collateral vein B Occlusion of venae comitantes of posterior tibial artery secondary to fracture (F) (AT) venae comitantes of anterior tibial artery (PT) venae comitantes of posterior tibial artery occluded at level of fracture Obstruction bypassed by arborizing collaterals

Venography is useful in several other situations When surgical ligation and sclerosing solutions have not controlled varicosities it may call attention to an incompetent communicating vein which is continually feeding the superficial vessels Similarly in the case of a varicose ulcer it may help locate the cause for venous stasis generally present in the vicinity of such a lesion It may also be of value in the study of chronic ulcers of the leg in which there is no apparent etiology since in this manner thrombosis of the deep venous system may be eliminated or implicated as a possible cause In the case of the upper extremity venography has a place in confirming the diagnosis of axillary vein thrombosis (Fig 3,B p 260) and of a block in other portions of the venous system (Fig 69)

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previously placed The free end of the polyethylene tube is passed through an air tight cork of a reservoir bottle so as to extend below the level of sterile heparinized saline solution half filling the container A mercury manometer* is connected by a three way stopcock to a sphygmomanometer hand bulb and to a glass tube which also pierces the cork of the reservoir bottle but reaches only to above the level of saline With such an arrangement, blood from the vein can flow into the polyethylene tubing but by adjusting the pressure this is checked A reading is obtained by raising the pressure in the system to above the anticipated venous pressure using the blood pressure bulb and then when the cannula is clear of blood lowering it very slowly The pressure is read on the manometer at the instant blood is noticed in the translucent tubing arising from the vein[1, 15]

Venous pressure readings in the lower extremities are obtained under three different conditions First the patient lies with the foot at heart level then he stands quietly erect and finally he walks briskly in place at a rate of one double step per second lifting his feet 6 inches from the floor

Clinical Application Normally venous pressure readings in the foot vary with the position of the body When the subject is lying down it is the same as the levels obtained in the upper extremity (4.4–8 8 mm Hg) On standing it rises considerably being equal to the pressure in recumbency plus an increment represented by the hydrostatic pressure of the column of blood between the right atrium and the point tested Depending on the height of the subject venous pressure varies between 70 and 100 mm Hg[1, 13] With exercise the pressure falls to around 30–40 mm Hg This sharp drop is due to the pumping action of the muscles on the neighboring thin walled veins propelling blood into the deep venous system and then out of the limb Reflux does not occur due to the action of competent valves

The presence of varicosities produces changes in venous pressure In recumbency the readings in the foot are generally higher than those of a normal subject probably because the existence of varicose veins over a period of time elicits an augmentation in circulating blood volume to compensate for the considerable pooling that occurs in the veins of the lower extremities in the upright position When the patient lies down these vessels are collapsed and as a result the amount of circulating blood is now greater than necessary to fill the vascular bed Consequently venous return and hence venous pressure increase[12, 13]

On standing the venous pressure in the lower extremity with varicosities is the same as that in a normal limb due to compensation in circulating blood volume After exercise however the drop ordinarily observed does not occur mainly because of regurgitation of blood from the deep venous system into superficial veins If a tourniquet is previously applied to the thigh to prevent this walking now reduces the pressure to normal levels

In the presence of a postphlebitic syndrome (Chap XVI) the readings in recumbency are normal but on standing they exceed the limits usually observed in this position Furthermore they do not decrease with exercise even when a tourniquet is applied Such responses in the upright position may be due either to a reflux of blood into the superficial venous system as a result of incompetency

* A water manometer can be substituted for the mercury manometer[2]

SOFT TISSUE X RAY TECHNIC

Technic Aside from its role in arteriography and venography, plain roentgenography has been used as an adjunct in the diagnosis of peripheral vascular disorders through its ability to demonstrate calcific changes in the wall of arteries Since the ordinary technic for the study of bony structure is not satisfactory a modification is utilized which heightens the contrast that exists among the several soft tissue densities of the part, such as fat and skeletal muscle and at the same time makes even minor calcium deposits visible on the film This consists of producing a 'softer' x ray beam, i e, one of longer than average wave length, through the use of 35–50 kv and a reduction in filtration to the minimum possible value (inherent filtration of the tube) The film exposure is adjusted by increasing the milliampere seconds to compensate for this thus obtaining a suitable film density

Clinical Application Soft tissue roentgenography is of value primarily in the visualization of the Monckeberg s type of arteriosclerosis * This finding may be helpful in differentiating arteriosclerosis obliterans from thrombo angiitis obliterans (p 137) Of course the mere presence of calcium in the media of a vessel without manifestations indicating a reduced local blood supply is not enough evidence on which to base a diagnosis of an occlusive arterial vascular disorder Conversely, the absence of calcification does not rule out this possibility, since atheromatous plaques, sufficient to produce definite interference with arterial inflow may be present in arteries and still not be identifiable on the x ray film

In some instances degenerative changes may occur in atheroma leading to hyalinization and later calcification The latter process is usually present deep in the intima near the base of the process It has a patchy plaquelike appearance and may be very dense varying in size from small round flecks of calcification to large irregular calcific densities 2 cm in size The large lesions can be visualized on the x ray as inconstantly distributed opacities along the course of an artery [1] In general, however the soft tissue x ray appears to have little or no practical value in the diagnosis of occlusive arterial vascular disorders and could be dispensed with entirely without the loss of really pertinent information

VENOUS PRESSURE MEASUREMENTS IN THE LOWER EXTREMITY

Technic Venous pressure determinations in the lower extremity require certain modifications of the standard procedure (p 65) among which is the use of a polyethylene tube instead of a needle Generally a superficial vein on the dorsum of the foot or in the vicinity of the ankle is surgically exposed under local anesthesia and cannulated by a #14 gauge thin walled needle Then a flexible polyethylene catheter, 30 cm (12 inches) long with an internal diameter of 1 mm is filled with isotonic saline solution and threaded through the needle into the vein The needle is now removed and the skin closed with one or two sutures

* *For a discussion of this clinical entity see Differential Diagnosis of Chronic Occlusive Arterial Vascular Disorders* Chap IX

PART THREE

ANATOMIC, PHYSIOLOGIC, PHARMACOLOGIC, AND PATHOLOGIC CONSIDERATIONS OF THE PERIPHERAL CIRCULATION

of valves in the deep veins, or to a block in a segment of the latter which prevents *the movement of fluid out of the limb* *

It would seem, therefore, that the determination of venous pressures in the lower *extremities in the upright position and on walking gives valuable data* regarding the function of the deep venous system First, it is objective and hence has a definite advantage over those procedures which are dependent on visual or tactile estimation of venous filling Second, it can be utilized despite lack of prominence of superficial veins or the presence of swelling or induration and brawniness of the skin, conditions under which the other clinical measures give little definite information Although the test may help differentiate primary varicosities from those secondary to deep thrombophlebitis, it is not recommended for routine application in uncomplicated varicosities

* Of diagnostic value is the fact that in certain conditions which may simulate the post phlebitic syndrome like lymphedema cellulitis or brawny induration of the lower extremities *standing and exercising venous pressures are normal*

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CHAPTER

XXVI ANATOMY AND PHYSIOLOGY OF BLOOD VESSELS IN THE EXTREMITIES

This chapter deals with the anatomy and physiology of the different components of the peripheral vascular system and the manner in which disease processes may affect them. Only those points are emphasized which have clinical implications or are essential for the better understanding of the altered structural or functional mechanisms responsible for peripheral vascular disorders. A more comprehensive discussion of the field can be found in textbooks of anatomy and physiology.

THE ARTERIAL SYSTEM

General Anatomy and Physiology

Large and Medium Sized Arteries

The large and medium sized arteries for the most part act as conduits to carry blood from the heart to the capillaries and normally do not play any significant role in regulating the amount of nutrition that actually reaches the tissues. However these vessels are affected by vasomotor impulses and hence under certain circumstances can go into spasm resulting in marked impairment of the peripheral circulation. They are also susceptible to structural changes of their walls which may permanently reduce their lumen and decrease the blood flow.

Arterioles

The arteriole is the terminal branch of the arterial tree. Under physiologic conditions provided cardiac output is normal it is the state of this vessel which determines the quantity of blood that passes through the capillary bed to nourish the tissues. With its thick muscular wall and its rich innervation of sympathetic fibers the arteriole is well adapted for this function. Besides smooth muscle the vessel also contains an endothelial layer and a thin adventitia.

Sympathetic tonus is particularly manifest in arterioles. As in other portions of the vascular system it is dependent upon vasoconstrictor impulses which arise in the vasomotor center and reach the peripheral vessels over the sympathetic

veins per unit of time is markedly reduced The fact that simultaneously there is constriction of the capillaries further decreases cutaneous blood flow However if the vasoconstricting stimulus is prolonged the arteriovenous shunts will open intermittently to permit arterial blood to come in contact with the tissues of the skin and thus tend to counteract any deleterious effect from the existing anoxia

There is some evidence to indicate that arteriovenous shunts may develop in response to the need for a local increase in blood flow and that when the circulation reverts to normal they disappear[4] These structures may also contribute to the relief of a very high pressure in the peripheral arterial system through their ability to shunt blood across to the veins In a similar fashion they may help reduce capillary stasis

The marked influence that the sympathetic nervous system exerts on the arteriovenous anastomoses permits ready lability in the mechanism of dilatation and constriction of these structures in accordance with body requirements In this function they supplement the action of the capillaries which are limited in their capacity to cope with extremes of temperature because of their relative paucity in the skin (see below)

Capillaries

The capillaries are the portion of the vascular tree in which the function of the circulation is consummated Here the interchange of metabolites and nutritive substances takes place for the purpose of serving the varying requirements of the fixed tissue cells The capillaries are also involved in the maintenance of a proper balance between tissue fluid volume and circulating blood volume

Anatomic Considerations A capillary loop forms the finest connecting link between the arteriole and venule being divided into a narrow arteriolar limb and a more dilated venular portion It is considered to be a vascular unit the caliber of which is sufficient to allow a row of red blood cells to pass through without causing any distortion of the cells and without these elements in turn producing any alteration in the shape of the vessel The capillary consists of an endothelial layer approximately 1 μ in thickness which is surrounded by a widely meshed network of Rouget cells These structures which may be undifferentiated muscle fibers were formerly believed to have physiologic significance by supplying the contractile element for the capillary[16] However it has since been shown that they play little role in this respect[5 30]

Certain diseases are associated with changes in capillary structure For example in polycythemia[2] and hyperthyroidism [4] the open capillary loops are significantly increased the vessels are widened and the total cross section of capillary bed is likewise enlarged In schizophrenia [1] and in neurocirculatory asthenia the cutaneous capillaries may be reduced in number while demonstrating irregularities in size and shape Abnormalities in capillary structure may also be seen in such disorders as scleroderma [1] and acrocyanosis the changes consist of the presence of unusually shaped loops minute aneurysms or saccular enlargements In severe cases of Raynaud s disease most of the capillaries appear enlarged

nervous system. If vasomotor tonus is decreased, as through the use of heat or with pleasant emotions, or if a block is produced in the peripheral sympathetic pathway, passive vasodilatation will occur in the arterioles, followed by an augmented local blood flow.

An increase in vasomotor tonus causes marked vasoconstriction and a reduced circulation. Such noxious stimuli as cold applied to distant portions of the body or pain act through the sympathetic nervous system to produce the same response. Most experimental evidence appears to support the view that the sympathetic nervous system exerts its greatest influence on the cutaneous arterioles particularly in the distal portion of the limb, while having little if any effect on those in the muscle. (For further discussion of this hypothesis, see *Variations in Normal Vasomotor Tonus,* Chap. XXVII.)

Blood flow through arterioles is also influenced by other factors. For example, epinephrine and pituitrin evoke vasoconstriction and a decreased circulation, in contrast to histamine and nitrites which elicit vasodilatation and an increased circulation. Physical exercise causes a marked augmentation in blood flow through muscle arterioles, as a result of locally accumulating metabolites and a greater cardiac output. Following a period of acute anoxia, cutaneous and muscle arterioles relax, also because of the dilating action of metabolites formed in tissues deprived of an adequate blood supply. This period of augmented circulation is called reactive hyperemia. (For further discussion of the subject see *Changes Occurring after Reversal of Experimental Anoxia,* Chap. XXVIII.)

Arteriovenous Anastomoses (Arteriovenous Shunts)

Anatomic Considerations. An arteriovenous anastomosis is a short vessel of approximately 0.02 mm. in diameter which establishes direct communication between the arterial and venous trees above the level of the capillary bed. It arises from a small artery and ends in a small vein. Its wall is three times as thick as that of an artery of similar sized lumen and its smooth muscle coat is richly innervated by nonmedulated sympathetic nerve fibrils. The afferent artery, the connecting loop, the neuroreticular and vascular structures around the canal, and the efferent veins collectively are called the glomus.* Beyond this structure the artery divides into smaller branches which ultimately terminate in the capillary bed. The shunts are found in greatest number in the distal portion of the extremities, particularly the nail bed of the fingers and toes,[10] and, to a lesser extent, in the thenar and hypothenar eminences. In females it may also be present in the forearms.

Physiologic Characteristics. The function of the arteriovenous shunts is to allow blood to enter the superficial veins without having to traverse the circuitous capillary pathway. Such an arrangement facilitates the loss of large quantities of heat from the blood to the environment. When there is need for conservation of heat, as on exposure of the body to cold, the arteriovenous shunts close and all the blood reaching the extremities must pass through the minute vessels of the capillary bed. As a result, the amount that can enter the superficial

* For discussion of an abnormal manifestation of a glomus, see *Glomus Tumor,* Chap. XXIII.

veins per unit of time is markedly reduced The fact that simultaneously there is constriction of the capillaries further decreases cutaneous blood flow However if the vasoconstricting stimulus is prolonged the arteriovenous shunts will open intermittently to permit arterial blood to come in contact with the tissues of the skin and thus tend to counteract any deleterious effect from the existing anoxia

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Certain diseases are associated with changes in capillary structure For example in polycythemia and hyperthyroidism[24] the open capillary loops are significantly increased the vessels are widened and the total cross section of capillary bed is likewise enlarged In schizophrenia[1] and in neurocirculatory asthenia the cutaneous capillaries may be reduced in number while demonstrating irregularities in size and shape Abnormalities in capillary structure may also be seen in such disorders as scleroderma[1] and acrocyanosis the changes consist of the presence of unusually shaped loops minute aneurysms or saccular enlargements In severe cases of Raynaud's disease most of the capillaries appear enlarged

Physiologic Considerations The size of the capillaries may be altered by various factors As in the case of the arteriole, the cutaneous capillary is innervated by nonmedullated sympathetic fibers stimulation of which produces contraction [11, 12] Local heat causes vasodilatation, a response which occurs even in the absence of sympathetic innervation

Vasodilatation of capillaries may be produced through a local axone reflex Involved in the response are nervous filaments which arise from cutaneous afferent nerve fibers and pass to nearby blood vessels When noxious agents are applied to the surface of the body, impulses are initiated which first spread centrally over afferent nerve fibers and then antidromically via axone collaterals to cause dilatation of the vessels through a cholinergic mechanism This type of response is lost when afferent fibers to the part degenerate It is possible that the so-called neurotrophic changes that occur in tabes dorsalis may be due to abolishment of the vasodilating mechanism initiated by an axone reflex, as a result of damage to the central terminals and to the dorsal root ganglia

Capillaries in the skin are exposed to a variable type of environment For example, they frequently come in intimate contact with such extraneous stimuli as extremes of heat and cold, ultraviolet light irradiation and trauma In contrast, capillaries in muscle are protected from such influences by virtue of their location some distance below the skin

Another difference is the fact that cutaneous capillaries besides their nutritive function are also involved in maintaining normal body temperature in the face of variations both in the amount of body heat produced and in the environmental temperature In fact, the metabolic needs of the skin may be partly sacrificed for a long time in order to accomplish this purpose On the other hand, circulation in muscle hardly plays any role in heat dissipation and conservation instead it follows more faithfully the metabolic needs of these tissues

Finally, it is important to point out that the number of cutaneous capillaries range between 16 and 65 per sq mm of cross section [17] while in the muscles there are between 1000 and 2000 for the same sized area [16] differences which can be correlated with variations in function For example the metabolic needs of muscle may vary markedly from time to time resting tissues requiring very much less nutrition than exercising ones Hence a mechanism is necessary which permits rapid changes in blood flow In contrast the nutritional requirements of the skin are much more constant so that there is less need for such a provision

Gross Anatomy of the Arterial Tree

Arteries of the Upper Extremity

Axillary Artery and Its Major Branches The main blood supply to the upper extremity is the axillary artery which gives off important branches to the shoulder region and then continues down the inner aspect of the arm as the brachial artery In the cubital fossa the latter divides into the ulnar and radial arteries (Fig 70) The ulnar artery courses down the ulnar side of the forearm to the wrist where it can usually be felt lateral to the pisiform bone (Fig 70) Just distal to this point, it divides into its larger superficial branch which contributes

strongly to the superficial volar arterial arch and a smaller branch which helps to form the deep volar arterial arch The ulnar artery also gives off the common interosseous artery which supplies the forearm and helps establish collateral circulation around the elbow (Fig 70)

The radial artery from its site of origin courses down the radial side of the forearm to the wrist where it is readily palpated near the proximal volar carpal skin crease It divides into two branches the superficial one continuing distally through the thenar eminence to the palm to contribute to the superficial volar

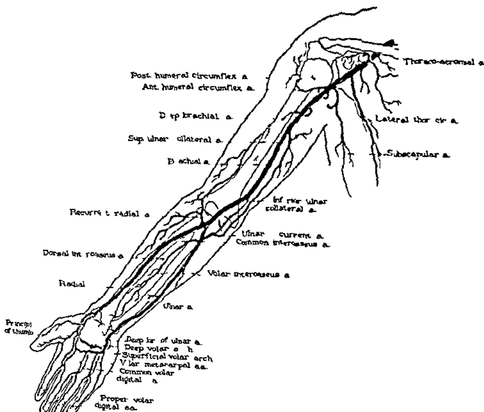


FIG 70 Arterial circulation in right arm forearm and hand

arch (Fig 70) The other much larger deep branch passes through the anatomic snuffbox and the first intermetacarpal space to reach the palm where it forms the greater part of the deep volar arterial arch (Fig 70) The fact that both arterial arches serve as connecting links or anastomoses between the ulnar and radial arteries is the basis for the ulnar confirmatory test (p 41) A line corresponding to the first transverse palmar crease marks the approximate location of the superficial volar arterial arch while the deep arch is a finger s breadth proximal to this location (Fig 70)

Blood Supply of the Hand The palmar surface of the hand is supplied in part by three common volar digital arteries which arise from the superficial volar

arterial arch and join the volar metacarpal arteries, branches of the deep volar arch, to become the digital arteries proper (Fig 70) The latter supply both sides of the third and fourth fingers, the ulnar aspect of the second finger and the radial aspect of the fifth finger The other side of the fifth finger receives its circulation directly from the superficial volar arch while the radial side of the *second finger and the thumb are supplied from* branches arising from the deep volar arch This pattern of distribution explains why, at times, the thenar eminence and thumb remain pale in the course of performing the ulnar confirmatory test even though the ulnar artery is intact For with the radial *artery compressed* digitally, evidently very little blood enters the deep volar arch, and hence the thumb from the patent ulnar artery This possibility must be considered in the interpretation of the results obtained with the test

The blood supply to the dorsum of the hand is derived from the dorsal carpal branches of the radial and ulnar arteries These anastomose to form the dorsal carpal rete, from which arise the second third and fourth dorsal metacarpal arteries The latter extend to the base of the fingers where they divide into the dorsal digital arteries to supply the digits However it must be pointed out that the main pathways for nutrition of the fingers is through the volar digital arteries *In Raynaud s disease both groups of vessels are involved in the temporary spasm*

Arteries of the Lower Extremity

Iliac Femoral, and Popliteal Arteries The arterial blood supply to the lower extremity is derived from the common iliac artery, which arises from the aorta at the level of the fourth lumbar vertebra and then divides into an external iliac and hypogastric artery *at the sacroiliac articulation The external iliac artery runs* downward over the psoas muscle to a point beneath the inguinal ligament, where it continues into the thigh as the femoral artery the main arterial channel of the lower extremity This vessel passes under the inguinal ligament, at which site its pulsations can be readily felt, to course down the anterior and medial aspects of the thigh and then through the tendinous opening in the adductor magnus muscle to reach the popliteal fossa

Near its origin and within the femoral trigone the femoral artery gives off the profunda femoris artery which supplies the muscles of the thigh From the latter vessel usually arise the lateral and medial circumflex femoral arteries, as well as *several perforator branches to the posterior muscles of the thigh In entering* the popliteal fossa at the back of the knee the femoral artery becomes the popliteal artery Below the popliteus muscle the popliteal artery divides into the anterior and posterior tibial arteries (Fig 71)

Anterior Tibial and Dorsalis Pedis Arteries The anterior tibial artery extends down the leg anteriorly and laterally between the tibia and fibula to reach the ankle joint where it becomes the dorsalis pedis artery The latter vessel in its course over the dorsum of *the foot has a* superficial location, thus permitting its examination for pulsations However the considerable variation of its course and branching[14] probably explains the difficulty in palpating this vessel in about 13 per cent of normal subjects In most instances the dorsalis pedis artery runs along

a line from a point halfway between the two malleoli to the posterior end of the first intermetatarsal space where it divides into the first dorsal metatarsal and the deep plantar arteries (Fig 72) In its course it gives off several branches the main one being the arcuate artery

The arcuate artery varies both in its origin and its length Generally it arises at the level of the first tarsometatarsal joint and extends laterally across the foot over the base of the metatarsal bones At the interspaces between the metatarsal bones

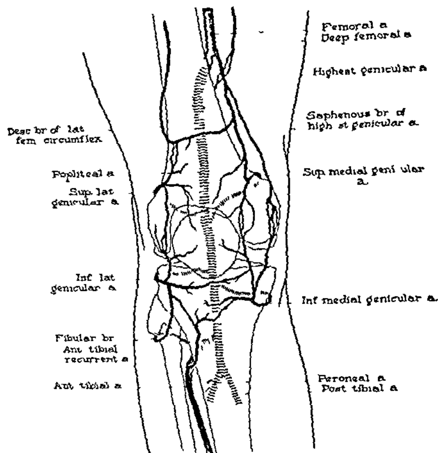


Fig 71 Arterial circulation around right knee

it gives off the second third and fourth dorsal metatarsal branches each of which divides into dorsal digital arteries The latter vessels supply the third to the fifth toes and the lateral aspect of the second toe while the medial aspect of this digit and the entire first toe receive their circulation from the first dorsal metatarsal artery (Fig 72) Occlusion of any of the branches supplying the digits may result in the appearance of nutritional disturbances

Posterior Tibial Artery This vessel extends downward over the medial and posterior portion of the leg first being deeply placed in the muscles of the calf and then becoming superficial and palpable near its termination between the

arterial arch and join the volar metacarpal arteries, branches of the deep volar arch, to become the digital arteries proper (Fig 70) The latter supply both sides of the third and fourth fingers, the ulnar aspect of the second finger, and the radial aspect of the fifth finger The other side of the fifth finger receives its circulation directly from the superficial volar arch, while the radial side of the second finger and the thumb are supplied from branches arising from the deep volar arch This pattern of distribution explains why, at times, the thenar eminence and thumb remain pale in the course of performing the ulnar confirmatory test even though the ulnar artery is intact For with the radial artery compressed digitally, evidently very little blood enters the deep volar arch, and hence the thumb from the patent ulnar artery This possibility must be considered in the *interpretation of the results obtained with the test*

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pulsation on the lateral and superior aspects of the ankle (Fig 3G p 43) In this site it may anastomose with the malleolar branch of the dorsalis pedis artery

Muscle Circulation In view of the frequent pathologic involvement of the arteries to the muscles of the lower extremities it is necessary to discuss their anatomic arrangement in more detail Generally each muscle group is supplied either by a series of arteries derived from a long segment of a major trunk or by one or a few branches arising in a sharply localized segment of the main channel[7] Examples of the former type of anatomic arrangement are found in the sartorius and vastus medialis which are supplied by the femoral artery and the tibialis anterior which receives its vascularization from the anterior tibial artery The muscles having a single or a few vessels are the rectus femoris receiving its nutrient vessels from the lateral circumflex femoral artery and each head of the gastrocnemius which is supplied by the popliteal artery[7]

There are certain characteristics of the circulation to the muscles of the lower extremities which make these structures vulnerable to ischemia[7] First the nutrient artery to a muscle group is usually an isolated unit having no substantial connection with vessels of neighboring structures Second even when there are multiple vessels, they usually enter at one localized site where injury could readily involve all of them simultaneously Finally there are generally no arterial anastomoses between vessels external to the muscles which they supply

ARTERIAL COLLATERAL NETWORKS

General Considerations

Of great prognostic significance in occlusive arterial vascular disorders are the compensatory mechanisms which come into play when the circulation through the normal arterial channels is reduced or interrupted Under these circumstances the function of maintaining an adequate state of nutrition to the tissues is taken over by the remaining patent vessels and by an enhanced collateral circulation

Mechanisms Involved in Production of a Collateral Network The effectiveness of the secondary vascular circulation is dependent upon a number of factors chief among which is the rate of obstruction of the main vessels If the lumen is suddenly occluded as by an embolus or immediately destroyed as by trauma there is relatively little time for an adequate collateral system to develop On the other hand a persistent but low grade state of impaired circulation permits the formation of an extensive secondary network

A second important point is the state of the other vessels at the time of occlusion of the main channel If they are patent and not involved in the occlusive process the possibility of obtaining an effective local blood flow is better than if many of them are partly obstructed

A third factor is the degree of existing tonus Sudden clo ure of a critical artery is generally associated with severe spasm of the remaining vessels a situation which produces a higher degree of anoxia At the same time this untoward response prevents hypertrophy of the main collateral branches and the development of accessory collateral channels If persistent and inten e it may even lead to thrombosis of normal vessels

medial malleolus and the calcaneus Here it divides into the medial and the strong lateral plantar arteries (Fig 72) The latter vessel courses laterally forward through the sole of the foot to the base of the fifth metatarsal bone and by curving toward the first metatarsal bone forms the plantar arch It terminates by anastomosing with the deep plantar branch of the dorsalis pedis artery From the plantar arch arise the plantar metatarsal arteries which follow a similar course to the dorsal metatarsal arteries by dividing into plantar digital arteries these also supplying the digits The other terminal branch of the posterior tibial artery, the

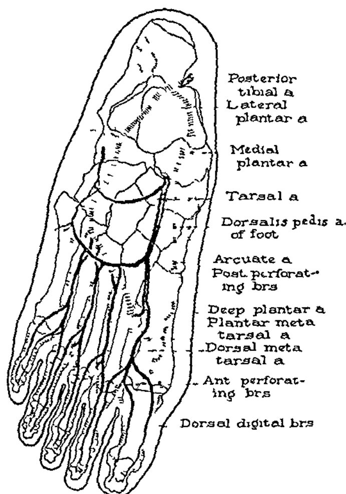


Fig 72 Dorsal and plantar arteries of right foot

much smaller medial plantar artery extends forward over the medial aspect of the sole of the foot Its anastomoses are variable and relatively less important

Near its origin from the popliteal artery the posterior tibial artery gives off its largest branch, the peroneal artery The latter crosses toward the fibula and then extends downward along the medial aspect of this bone It divides into lateral malleolar and calcaneal branches that run superficially over the lateral malleolus to the heel When the posterior tibial artery is occluded in some instances a perforating branch of the peroneal artery enlarges and can be felt as a prominent

of the branches of the subscapular a subdivision of the axillary, and the transverse cervical and transverse scapular arteries of the thyreocervical trunk Another branch of the axillary artery, the lateral thoracic artery, also communicates with the internal mammary and intercostal arteries and with the pectoral branch of the thoracoacromial artery (Fig 70) (For a discussion of axillary artery embolism, see p 153)

Occlusion of the Lower Portion of the Brachial Artery The secondary circulation around the elbow is so extensive that obstruction of the brachial artery at its

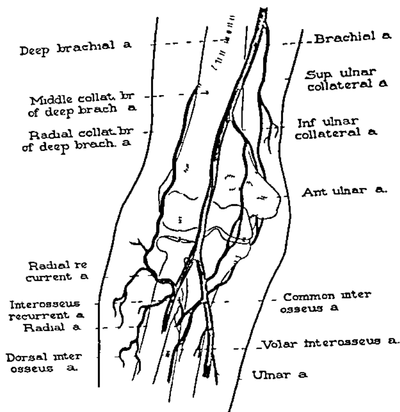


FIG 73 Collateral arterial circulation around right elbow

bifurcation is usually followed by no untoward effects Involved in the collateral network is the anastomosis behind the medial condyle of the superior ulnar collateral artery a branch of the brachial artery with the posterior ulnar recurrent artery arising from the ulnar artery (Fig 73) Another communication occurs between the inferior ulnar collateral from the brachial artery and the anterior ulnar recurrent a branch of the ulnar artery This takes place in front of the medial condyle On the lateral side an anastomosis is formed between the anterior radial collateral a branch of the profunda brachii artery and the radial recurrent artery arising from the radial artery Finally the posterior radial collateral

Another factor which influences the efficiency of a collateral circulation is the site and extent of obstruction It is obvious that if thrombosis occurs in a large vessel at the point of origin of one or several collateral branches, the blood supply to the tissues distally will be further jeopardized Moreover, the longer the extent of the block, the greater are the chances of involving additional orifices of collateral branches [15]

Finally, the type of occlusive arterial disease plays a role If it is self limiting the *prognosis is fairly good* whereas *the possibility* of maintaining an adequate circulation is reduced when the occlusive process tends to extend into new channels In general, it can be stated that tissues will not suffer from lack of nutrition *provided the sum of the squares of the diameters of the patent collateral vessels* is at least equal to the square of the diameter of the occluded main artery

Derivation of Secondary Network Collateral channels have several origins Normally there are secondary branches in some crucial areas which are already functioning and which, as a result of the added stimulus, now dilate and anastomose with one another (main collateral branches) A rather constant finding is the enlargement of a pre-existing branch which arises proximally to the block, passes at right angles to the main channel, then turns to run parallel with it, and finally joins it distally

Another set of vessels consists of small and irregularly distributed arteries which are found primarily in muscles (accessory collateral branches) [1] Whether these are newly formed or always present but not functioning has not been determined There may also be supplementary branches, which originate from either main or accessory collateral channels and generally run parallel to the obliterated artery Twigs from the main collateral branches may form bridging pathways around the site of occlusion If the obstruction occurs in the terminal portion of an artery *small collaterals may arise proximally to the involved site and pass distally* in an approximately parallel course to the occluded vessel Another mode for developing collateral circulation is prolongation of a main artery so that its branches will *now supply an area previously provided for by* the subdivisions of the obliterated vessel

Conditions Leading to the Formation of Secondary Network Of the various factors implicated in the growth of a collateral circulation the most potent appears to be a state of chronic anoxia It has been suggested that the actual mechanism involved under these circumstances is a chemical stimulant arising in tissues deprived of an adequate oxygen supply [19] Although the height of the blood pressure plays a role in arterial growth, it is not nearly so important as the difference between the pressure in the normal vessels and that in the vascular bed of an ischemic area This factor is evidently responsible for the subsequent dilatation of the collateral channels *Other contributing and significant influences in the* formation of a secondary network are the age of the patient, the general condition of the heart, and the viscosity of the blood

Collateral Arterial Networks Resulting from Obstruction of Specific Vessels

Occlusion of the Axillary Artery If the axillary artery is occluded in its middle portion a usually adequate collateral circulation will be established by anastomoses

THE VENOUS SYSTEM

General Anatomy and Physiology

Venules

Anatomic Considerations The venules differ from the capillaries being larger and containing a definite connective tissue coat external to the endothelium Rouget cells are occasionally noted In the skin venules are present in the form of four layers the first being located at the base of the papillary layer of the dermis and receiving blood from the capillaries and collecting venules It freely communicates with the next one the two together forming the subpapillary venous plexus The third layer lies beneath these two while the fourth is at the junction of the dermis and the subcutis The blood in the subpapillary venous plexus contributes to a great degree to the normal skin color (For further discussion see *Factors Responsible for Normal Skin Color* Chap XXVIII)

Physiologic Considerations The cutaneous venules have several functions First their thin walls offer a large total surface for the interchange of water and dissolved substances between the tissues and the circulating blood Because of this the vascularity of the skin is greater than the number of true capillaries would indicate since the subpapillary venous plexus may take over part of the normal function of the capillary bed if the necessity arises The subpapillary venous plexus may also serve as an important blood reservoir It is capable of accommodating variable amounts of blood when there is need for a reduction in circulating blood volume and returning it to the circulation through the mechanism of venoconstriction when the emergency no longer exists [3]

Venules have the ability to contract independently of blood vessels in other portions of the vascular tree the responsible mechanism evidently being the endothelium rather than the Rouget cells Cutaneous venules become actively constricted by gentle stroking of the skin (white reaction) while firm stroking with a blunt instrument produces active relaxation (red reaction) Such responses occur even in the absence of nervous innervation [17 18]

Veins

Veins are generally thinner than arteries of similar size because of the small quantity of muscle and elastic tissue in their wall In a medium sized vein the media consists mainly of circular smooth muscle fibers separated by many longitudinal collagenous fibers and some fibroblasts However in the case of the veins of the lower extremity this layer is much thicker resembling more nearly that of arteries

As in the case of the different segments of the arterial tree veins possess muscular tone which is dependent upon the integrity of the sympathetic nervous system This function is noted chiefly in cutaneous vessels [6] which contract on exposure to various types of noxious stimuli and chemicals such as cold applied

from the profunda brachii artery communicates posteriorly with the interosseous recurrent artery, a branch of the dorsal interosseous artery The latter arises from the common interosseous artery, a subdivision of the ulnar artery

Occlusion at the Aortic Bifurcation Slow occlusion of the aorta at the bifurcation may result in at least a temporarily adequate circulation to the lower extremities Such a situation is frequently noted in Leriche s syndrome (p 166) in which trophic changes may be absent in the feet for many years despite the fact that all the blood flow reaching the limbs must pass through collateral vessels This is in contrast with sudden occlusion of the aortic bifurcation, which almost invariably is followed by gangrene in one or both lower extremities (Chap X)

The collateral channels that develop after progressive obstruction of the aortic bifurcation will vary in different individuals A common finding is the presence of dilated, tortuous intercostal arteries anastomosing inferolaterally with the deep circumflex iliac branch of the external iliac artery Enlargement of the two lower intercostal and iliolumbar branches of the hypogastric artery also occurs, thus permitting blood to enter the internal iliac artery Collateral channels between the lumbar arteries and the deep circumflex iliac arteries as well as with the iliolumbar arteries are frequently noted in the paravertebral regions Within the rectus abdominis muscle anastomoses will be found connecting the superior epigastric branch of the internal mammary with the inferior epigastric branch of the external iliac artery

Occlusion of the Femoral Artery After obstruction of this vessel a collateral circulation is possible through a number of channels The superior and inferior gluteal branches of the hypogastric artery anastomose with the medial and lateral femoral circumflex and first perforating branches of the profunda femoris artery Another branch of the hypogastric artery the obturator artery, joins with the medial femoral circumflex branch of the profunda femoris artery The internal pudendal branch of the hypogastric artery communicates with the superficial external pudendal branch of the femoral artery Finally the deep circumflex iliac artery a branch of the external iliac artery joins with the ascending branch of the lateral femoral circumflex artery a subdivision of the profunda femoris artery

Occlusion of the Popliteal Artery After closure of this vessel, the circulation to the leg and foot is carried on through the collateral channels around the knee (Fig 71) The highest genicular artery a branch of the femoral artery and the descending branch of the lateral femoral circumflex artery anastomose with the inferior lateral and medial genicular and superior medial genicular arteries These connections form the circumpatellar rete which is joined from below by the anterior tibial recurrent artery It is questionable as to whether this collateral network is always functionally effective after occlusion of the popliteal artery In comparison, the collateral circulation around the elbow appears much more adequate (Fig 73) Such differences may possibly be related to the fact that the leg and foot make up a much greater mass of tissue than do the forearm and hand and hence their metabolic requirements are much higher

the elbow, the basilic vein receives the variable median cubital vein (median basilic vein) a tributary of the cephalic vein (Fig 75) A third inconstant superficial venous channel the median antibrachial vein arises in the volar venous arches extends upward on the volar surface of the forearm, and terminates either in the basilic or in the median cubital vein

The vessels of the superficial venous system may at times manifest a thrombophlebitic process particularly those in the cubital space, a location which is readily accessible for diagnostic and therapeutic venipuncture

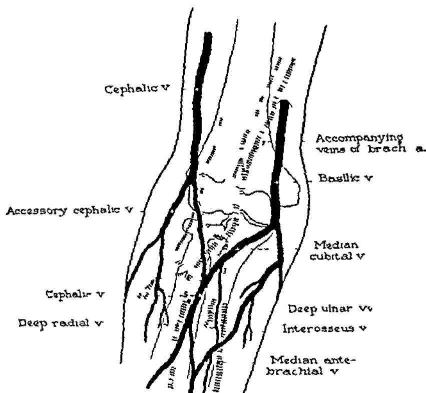


FIG 75 Venous circulation around right elbow

Deep Venous System This network has its origin in the small digital veins which empty into the volar superficial and deep venous arches each of the latter being associated with the corresponding arterial arch The venous arches are continued upward onto the forearm as the venae comitantes of the ulnar and radial arteries At the elbow these vessels combine to form the venae comitantes of the brachial artery which in turn unite with the basilic vein to form the axillary vein The latter vessel increases in size as it ascends by receiving tributaries corresponding to the branches of the axillary artery Other channels which enter it are the cephalic the long thoracic and the thoracoepigastric veins The axillary vein lies within the axillary sheath together with the axillary artery and the cords and branches of the brachial plexus As it approaches the apex of the axillary

to distant portions of the body, epinephrine, paredrine, and paredrinol Nitri and heat produce inhibition of venous tonus

Gross Anatomy of Venous System

Superficial and Deep Veins of the Upper Extremity

Superficial Venous System This network originates as digital veins draini into the dorsal venous arch, a very prominent venous network on the dorsum

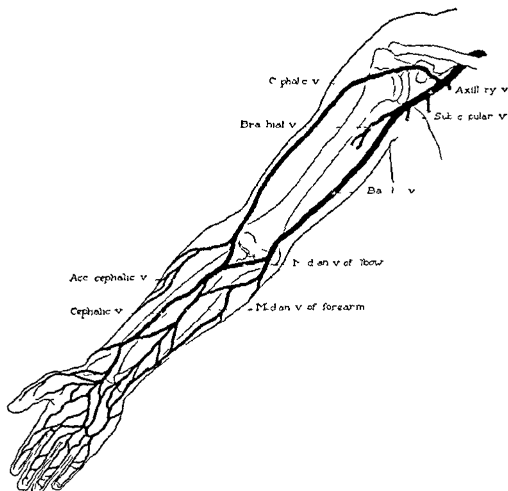


Fig 74 Superficial venous system of volar surface of right arm fore arm and hand

the hand From the radial side of the arch arises the cephalic vein which course upward over the lateral aspect of the forearm and arm and in the upper thi of the latter passes between the pectoralis major and deltoid muscles It terminate in the axillary vein just below the clavicle (Fig 74)

The second main superficial channel the basilic vein originates from the dorsa venous arch on the ulnar side of the hand and courses up the medial aspect of th forearm It pierces the deep fascia of the arm in its lower medial third and at th axilla contributes to the formation of the axillary vein (Fig 74) At a point belov

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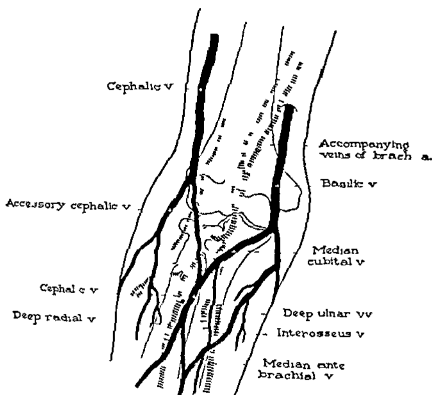


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fossa, the axillary vein is the most medial of these structures Its continuation is the subclavian vein (Fig 76)

Superficial and Deep Veins of the Lower Extremity

Superficial Venous System This network, composed of the great and small saphenous veins and their tributaries, drains blood from the skin and subcutaneous tissues of the entire lower extremity (Fig 77) A comprehensive knowledge of the anatomic locations of the superficial venous system is essential in the surgical treatment of varicosities (Chap XIII)

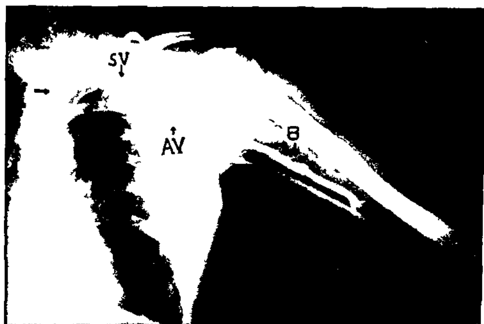


Fig 76 Normal venous tree in upper extremity outlined by venography (*B*) basilic vein (*AV*) axillary vein (*SV*) subclavian vein (*IV*) innominate vein

The superficial drainage of blood from the foot begins with the dorsal digital veins which course upward to become the short common digital veins the latter uniting to form the dorsal venous arch From the medial aspect of the dorsal venous arch arises the great saphenous vein (V saphena magna) (Figs 77 and 78) This vessel extends upward in front of the medial malleolus and then along the medial aspect of the leg and knee and the medial and anterior surfaces of the thigh It passes through the fossa ovalis below the inguinal ligament to end in the femoral vein In its course it receives numerous tributaries draining blood from the medial portion of the foot, leg and thigh

Distal to its entrance into the deep venous system the great saphenous vein is joined by a number of constant tributaries One of these the superficial circumflex iliac vein, receives blood from the lower and lateral parts of the abdominal wall and the proximal and lateral portions of the thigh Another the superficial epigastric vein drains the lower and medial aspects of the abdominal wall A

third the superficial external pudendal vein receives blood from the dorsum of the penis and the scrotum in the male and from the labium majus in the female

At least two other vessels enter the great saphenous vein in the same region but somewhat more distally One is the lateral superficial femoral vein which ascends from the lateral side of the knee and courses medially and anteriorly over the lower thigh while the other is the medial superficial femoral vein, which runs along the posterior and medial aspects of the thigh Although these vessels lie

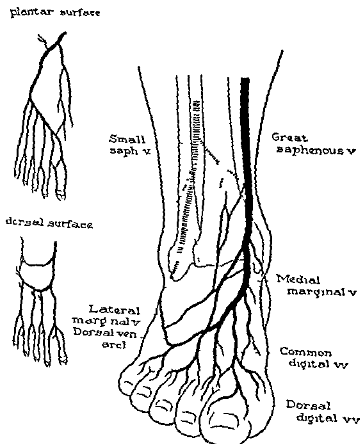


Fig 77 Superficial venous system of right foot

more superficially than the great saphenous vein it is at times difficult to distinguish them from the main venous channel (For the role of the above described veins in the formation of varicosities see p --- for their importance in the surgical treatment of this condition see p 230)

The small saphenous vein (V saphena parva) begins in the dorsal venous arch but on the lateral side of the foot (Fig 77) It is shorter than the great saphenous vein although it receives many tributaries which drain blood from the superficial tissues of the posterior and lateral portions of the foot and leg It ascends behind the lateral malleolus and onto the posterior surface of the calf to pass through

the deep fascia and finally into the popliteal vein This junction usually occurs at a level somewhat above the flexion crease of the *popliteal space* (Fig 78) The fascial penetration can occur at any point between one third and two thirds of the distance from the popliteal crease to the ankle joint,[3] an anatomic variation to be kept in mind when seeking for varicosities of the small saphenous vein

Deep Venous System This portion of the venous tree originates in the plantar plexus of veins located in the small muscles of the foot (Fig 77) From the latter

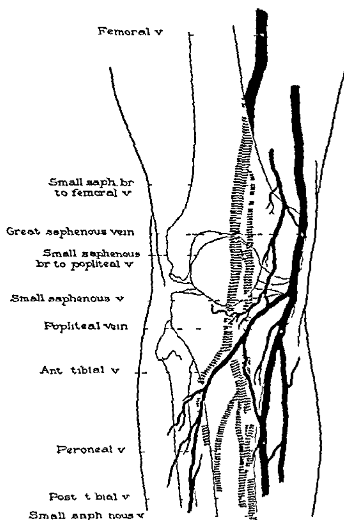


Fig 78 Venous circulation around right knee

venous network arise the plantar digital veins which unite to form the metatarsal veins and then enter the deep plantar *venous arch* The *venae comitantes* of the posterior tibial artery after their origin in the deep plantar venous arch ascend the leg to join the venae comitantes of the peroneal artery These vessels are then united with the venae comitantes of the anterior tibial artery near the upper border of the interosseous membrane to form the popliteal vein The venae comitantes of the posterior tibial artery drain the venous plexuses of the muscles of the foot and calf which are potential sites for the production of pulmonary emboli The venae comitantes of the anterior tibial artery receive *blood from the*

anterior portion of the leg and are continuations of the venae comitantes of the dorsalis pedis artery (Fig 79A)

The popliteal vein may arise as a single channel or as two or even three separate trunks A double vessel arrangement is the most frequent [8] a finding which has

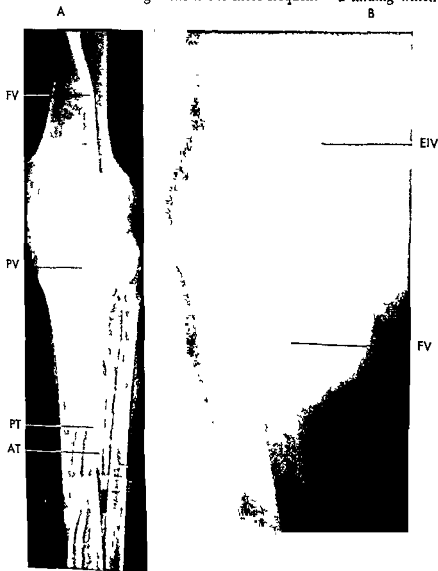


FIG 79 Normal venous tree in lower extremity outlined by venography A (PT) venae comitantes of posterior tibial artery (AT) venae comitantes of anterior tibial artery (PV) popliteal vein (FV) femoral vein B (FV) femoral vein (EIV) external iliac vein

clinical significance if therapeutic ligation of the popliteal vein is contemplated This vessel passes through the popliteal space first being medial to the popliteal artery and then superficial to it The vein continues upward through the adductor hiatus to become the femoral vein (Fig 79B) The latter passes beneath the in

guinal ligament, now lying medially to the femoral artery, to emerge as the external iliac vein. The common iliac vein is formed by the union of this vessel and of the hypogastric vein at the level of the sacroiliac joint. The inferior vena cava, in turn, is formed by the junction of both common iliac veins. It courses over the lumbar vertebrae to the right of the abdominal aorta.

In the thigh the femoral vein receives a number of large tributaries which, for the most part, are venae comitantes corresponding roughly to the muscular branches of the femoral artery.[9] The most inferior vessel is the deep femoral vein (companion vein of the deep femoral artery), which is formed by the fusion of the lower and upper perforating veins of the thigh and which drains the muscles in this location. It joins the main venous channel about 8 cm. (approximately 3 inches) below the inguinal ligament.[9]

In about 10 per cent of cases a large communication exists between the deep femoral vein and the lower portion of the femoral vein,[9] an anatomic finding which has clinical implications. For, under such circumstances the commonly used procedure of ligation of the femoral vein, below its junction with the deep femoral vein, would not necessarily prevent emboli arising at a lower level in the deep venous system from entering the inferior vena cava.

Other large channels which enter the femoral vein are the lateral femoral circumflex and the medial femoral circumflex veins. The first joins the vessel above the entrance of the deep femoral vein, and the other, at an even higher level, at the point where the great saphenous vein terminates in the femoral vein. The lateral femoral circumflex vein may be present as two or three vessels which enter the femoral vein separately, while the median femoral circumflex is generally single.

Perforating or Communicating Veins

In both the upper and lower extremities there are numerous communicating veins which unite the deep and superficial venous systems at various levels. Since destruction or incompetency of the valves in such vessels in the lower extremities generally leads to the production of varicosities in the group of superficial veins drained by them, a knowledge of their location is essential, especially if surgery is contemplated.

The communicating veins in the lower extremity have a fairly constant location and on this basis can be divided into several main groups: the muscular perforators in the calf, the small saphenous system, the vessels on the medial and lateral aspects of the leg, and those on the lateral side of the foot. In the region below the knee there are generally numerous small communicators which penetrate the deep fascia in the calf. A larger vessel may also join the upper segment of the vena comitantes of the posterior tibial artery with the small saphenous vein.

Of special clinical interest are three relatively large and constant perforators which drain behind the medial malleolus the ulcer-bearing area. The upper one usually establishes a large communication between the great saphenous vein and the venae comitantes of the posterior tibial artery, while the other two drain the subcutaneous tissues of the medial aspect of the lower portion of the leg and

enter the deep veins directly There are also communications with a constant branch of the great saphenous vein which arises at the level of the knee and passes distally to form a posterior venous plexus

The fact that the perforators in the vicinity of the medial malleolus pass out through tendons and are not supported by the muscles as are the ones higher in the leg, may also contribute to their vulnerability to pathologic alterations [6] In the presence of incompetency of these vessels, a great strain is placed on the fine venous network of the subcutaneous tissues which they drain It is quite possible, therefore that such a situation exists when ulcers form in this region

Venous Valves

Venous valves play a very important role in the function of venous return especially in the case of the lower extremities These structures are generally found at the junctions of tributaries with main venous channels or where two large veins join As a result backflow of blood into vessels of lower pressure is prevented Valves in communicating veins are instrumental in directing the movement of blood toward the deep venous circulation Congenital absence of valves between the heart and the great saphenous vein predisposes to venous stasis and the development of superficial varicosities Similarly, their destruction or a reduction in their number in the deep venous system results in excessive strain on the remaining ones possibly with the production of incompetency The most common site of pathologic involvement of venous valves is the superficial system or the perforator veins

Structure Venous valves are generally bicuspid and occasionally tricuspid The cusp is composed of collagenous fibers smooth muscle and elastic tissue the whole structure being covered by endothelium [8] The collagenous fibers are numerous at the base but more sparsely distributed toward the free edge of the cusp muscle is also found at the base being continuous with the longitudinal fibers of the wall of the vein To the outer side of each cusp lies the dilated valve sinus The space between the cusp attachments is the commissural region the wall being thickened in this area to form a distinct projection into the lumen [8]

Histologic examination of abnormal valves from a varicose saphenous vein generally reveals no profound intrinsic lesions The change in most instances is a dilatation of the commissural region producing an evagination of the wall and a separation of the cusps Associated with these alterations may be secondary changes of a corrective nature consisting of a growth of fibromuscular tissue into the lumen surface of the dilated commissure The [illegible] ... ow some [illegible] ... ing and

[illegible] numerous in the deep veins of the legs and thighs with a somewhat lesser number in the superficial system In about one third of the cases a single valve is found in the external iliac vein distal to its junction with the internal iliac vein In three quarters of the cases the femoral vein shows a set of valves at the level of the inguinal ligament Valves are almost always present in the lower segment of the femoral vein [3] ranging in number

from one to four, with a constant one situated just distal to the junction with the deep femoral vein A valve in the upper part of the popliteal vein is also fairly constant

In the upper extremity, the deterrent effect on venous return of hydrostatic pressure in the upright position is much less serious than in the lower extremity As a result, there is a relative paucity of venous valves A pair is present in the axillary vein, opposite the lower border of the subscapularis muscle and another at the termination of the cephalic and of the subscapular veins

Venous Collateral Networks

Almost immediately following occlusion or ligation of a major vein in an extremity, compensatory changes occur in the venous system which facilitate drainage of blood from the involved limb First among the factors influencing the production of a secondary venous network is *the rate of occlusion of the vessel*, an acute obstruction being followed by a less effective collateral circulation than a gradual one The size of the involved vein, the number of its branches similarly occluded by the process, the level of obstruction, the degree of existing vasospasm, and the demands placed on the *venous circulation locally by physiologic activity* will also influence the subsequent course

In general the changes consist of dilatation of tributaries and the formation of new collateral vessels, derived from pre existing veins and venules Most of the secondary channels *develop in the superficial structures underlying the skin* since the tissue pressure in the deeper layers of the extremity are sufficiently high to discourage such a tendency at these sites [76]

Collateral Venous Networks Resulting from Obstruction of Specific Vessels

Occlusion of the Superior Vena Cava The gradual obstruction of this vessel results in the formation of an extensive superficial collateral network * In most instances *the resulting pathway will depend upon the relationship of the occlusion* to the azygos vein This vessel ascends alongside the vertebral column and enters the superior vena cava as its last tributary Hence it can serve as an alternate route when the main vein is obstructed

If the occlusion occurs above the entrance of the azygos vein into the superior vena cava then a large part of the blood from the upper half of the body can be collected by the azygos vein and returned to the vena cava proximal to the obstruction The secondary pathways utilized under such circumstances are similar to *those that follow closure of both innominate veins* [13] *On each side blood* passes from branches of the external jugular and lateral thoracic veins into the tributaries and the stem of the internal mammary vein and from there into the superior vena cava via the intercostal hemiazygos and azygos veins As a consequence, a *plexus of dilated veins becomes apparent on both sides of the* anterior chest wall

If the occlusion occurs below the entrance of the azygos vein into the superior vena cava, the above collateral pathway is not available Instead the flow in the azygos vein is reversed in direction This vessel now receives much of the normal inflow to the superior vena cava *and then reroutes it via collaterals* so that it

* For discussion of superior vena cava syndrome see Chap XXIV

enters the inferior vena cava and the right atrium At least two pathways can be used One consists of the internal mammary the lateral thoracic, the thoracoepigastric the inferior epigastric the saphenous and the iliac veins, in that order while another involves the superior and inferior epigastric and the iliac veins Associated with such an aberrant flow of blood is the formation of a pattern of dilated superficial veins extending from the anterior and lateral thoracic walls to the lower abdomen (Fig 66 p 392)

If obstruction involves the azygos vein itself the collateral circulation must now depend upon the superficial veins and the vertebral system of veins which generally are not as effective as in the case of the other two locations

Occlusion of Axillary or Subclavian Vein* Following such a pathologic change a collateral venous system is also rapidly established (Fig 33 p 260) This consists of anastomoses between tributaries of the subscapular branch of the axillary vein and the transverse cervical and transverse scapular branches of the thyreocervical veins The lateral thoracic vein may also play a role by its connections with the internal mammary and intercostal veins Other important collateral pathways involve communications of the cephalic vein with the internal mammary and external jugular veins

Occlusion of the Inferior Vena Cava The lack of symptoms following ligation or thrombosis of the inferior vena cava is attributed to the rich collateral venous circulation which is set up soon after continuity of the vessel is destroyed This is considered to be similar to that which follows division of the common iliac veins It involves the shunting of blood from the saphenous system to the superficial [illegible] the superficial

[illegible] pathway is the communications between the external iliac and the internal mammary and ascending lumbar veins through the anastomosis of the deep circumflex iliac and the deep inferior and superior epigastric veins Two large ascending lumbar veins on each side likewise play a role in removing the blood from the common iliac veins through their connection with the superior vena cava via the azygos system and hemiazygos veins

Occlusion of the Femoral Vein When ligation of the femoral vein is carried out either as a prophylactic [illegible] treatment of phlebothromb[illegible] mechanism which comes [illegible] adequate venous return depends upon the site of ligation

If the interruption occurs below the termination of the deep femoral vein very little venous obstruction results since this vessel has good anastomatic connections If ligation is performed above the termination of the deep femoral vein but below the entrance of the lateral and medial femoral circumflex veins interference with venous outflow is much greater The available venous channels consist of a chain of veins in the posterior portion of the thigh which is formed by the deep femoral vessels and which enters both femoral circumflex veins and the inferior gluteal veins[9] There may also be some return through the obturator vein leading into the hypogastric and hence the common iliac vein

The largest amount of blood is trapped in the lower extremity when interruption

* For a discussion of primary thrombosis of axillary vein see Chap XIV

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* For discussion of superior vena cava syndrome see Chap XXIV

Anatomy of Lymphatic Network of Lower Extremity

As in the case of the upper extremity in the lower extremity the lymphatic vessels form a superficial and a deep system with the popliteal and inguinal lymph nodes acting as the only communication between them Most of the superficial lymphatics of the foot and leg terminate in the popliteal lymph nodes From the latter arise large efferent trunks which course along with the femoral vessels to end in the external iliac nodes just distal to the bifurcation of the aorta Many of the superficial lymphatics of the upper part of the leg and the entire thigh enter the inguinal lymph nodes from which arise other channels which also drain into the external iliac nodes

The lymphatics of the deeper set in the lower extremity originate as networks in the muscle sheaths which then unite to form larger vessels Some of these from the foot and leg enter the popliteal lymph nodes while those arising in the thigh become tributaries of trunks which eventually drain into iliac nodes The large vessels are found in close proximity to the main veins and are enclosed in a tough fibrous sheath

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of the femoral vein occurs above the level of entrance of the great saphenous and both femoral circumflex veins. The only obvious route that now exists to bypass the obstruction consists of anastomoses of the medial femoral circumflex vein with the obturator and inferior gluteal veins. Another pathway which could possibly be utilized is the communication with the hypogastric vein through the dorsal vein of the penis and the internal pudendal vein.[11]

LYMPHATIC SYSTEM

The anatomy and physiology of the lymphatic system are poorly understood. The lymphatic channels form a distinct, closed network of endothelial walled vessels, not related either to the serous cavities or the connective tissue spaces. The lymphatic system originates as a meshwork of delicate vessels (lymph capillaries) which drain the tissue spaces. The small channels are joined by others, forming larger ones, which in turn receive tributaries along their course. The vessels gradually increase in size finally to form the right lymphatic and thoracic ducts which pour their lymph into the blood stream by way of the right and left subclavian veins respectively. The large lymphatic channels are well supplied with valves and are generally found accompanying main veins. Their course can not be described as readily as that of the arterial or venous tree, since their location is not as consistent.

Strategically placed in regard to the pathway of the main lymphatic channels are lymph nodes into which the vessels enter and then break up to form a fine network. After passing through the nodes the lymphatic vessels re-form into a few larger trunks. The nodes are found at the elbow, the axilla, the knee and the groin where they act as a barrier against the entrance of deleterious agents, particularly bacteria, into the blood stream. They may also contribute toward the body's defense by the production of antibodies.

Anatomy of Lymphatic Network of Upper Extremity

In the hand most of the lymph from the palmar aspects of the fingers, web areas and hypothenar and thenar eminences flows into a large number of superficial lymphatic channels located in the loose areolar layer on the dorsum. This accounts for the marked lymphedematous swelling frequently seen on the back of the hand even when the focus of infection is in the palmar aspect. The lymph leaves the dorsum of the hand by way of lymphatic channels which accompany the basilic and cephalic veins. Those on the medial aspect of the forearm end or pass through the cubital lymph nodes. The lymphatic vessels which follow the cephalic vein course uninterruptedly over the forearm and arm and then drain into the axillary nodes or, less frequently, the deltopectoral or supraclavicular nodes.

The deep lymphatic channels of the arm run with the large deep veins and also empty into the axillary nodes with or without first communicating with the deep cubital nodes. Connections between superficial and deep lymphatic channels occur at the elbow via the deep and superficial lymph nodes.

ANATOMY OF LYMPHATIC NETWORK OF LOWER EXTREMITY

As in the case of the upper extremity in the lower extremity the lymphatic vessels form a superficial and a deep system with the popliteal and inguinal lymph nodes acting as the only communication between them Most of the superficial lymphatics of the foot and leg terminate in the popliteal lymph nodes From the latter arise large efferent trunks which course along with the femoral vessels to end in the external iliac nodes just distal to the bifurcation of the aorta Many of the superficial lymphatics of the upper part of the leg and the entire thigh enter the inguinal lymph nodes from which arise other channels which also drain into the external iliac nodes

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CHAPTER

XXVII SYMPATHETIC NERVOUS SYSTEM

The sympathetic nervous system by means of its control over the blood vessels in the extremities plays an important role in the regulation and distribution of the available circulating blood This is particularly true when the position of the body is altered or when there is need for heat dissipation or conservation (p 456) In the present chapter are presented the pertinent anatomic facts relating to the origin of vasoconstrictor impulses and the pathways taken by them to reach the neuroeffector cells in the blood vessel wall Also included is a discussion of the various factors responsible for normal increased and decreased vasomotor activity, the portions of the limbs in which sympathetic control predominates and the changes produced when this influence is temporarily or permanently removed

CENTERS AND PATHWAYS INVOLVED IN VASOCONSTRICTION

Central Control of Vasomotor Tonus

There is little question that higher centers in the brain exert some control over sympathetic activity but the exact location of such centers has not been clearly defined That the cerebrum is implicated is supported by the finding that emotions such as fear pain embarrassment and excitement are associated with vasomotor responses The hypothalamus also plays an important role in the control of vasomotor activity Projection systems arise within it which descend to make synapse either with sympathetic medullary centers or directly with sympathetic motor neurons located in the intermediolateral column of the spinal gray matter[1] In the cord these vasomotor fibers lie ventral to the lateral corticospinal tract and between it and the anterior horn of the gray matter

Peripheral Pathways*

From the cell bodies in the intermediolateral column arise preganglionic fibers which pass from the cord through the anterior roots and reach the paravertebral sympathetic ganglia by way of the white communicating rami In the ganglionic chain they pass for varying distances before each fiber makes synapse with up to 20 postganglionic neurones The postganglionic vaso constrictor fibers leave the ganglionic chain via gray communicating rami to enter peripheral mixed nerves

* Figure 80

and are then distributed to the arterial and venous systems in the extremities These sympathetic elements consist of nonmedullated fibrils which end in the adventitia of the blood vessels by forming perivascular strands of plexuses From the latter, secondary fibers arise which penetrate the media and give off smaller fibrils, ultimately terminating in proximity to muscle cells Sympathetic twigs are present in large numbers in the vicinity of arteries, arteriovenous shunts, and arterioles, while the innervation of veins and capillaries is much less profuse

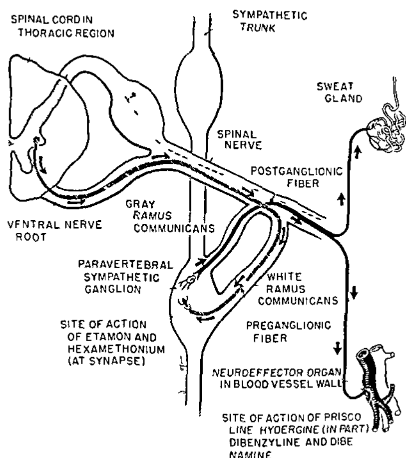


Fig 80 Diagram of peripheral sympathetic pathways, with sites of action of sympathetic blocking agents indicated (From D I Abramson Surgical physiology of peripheral arterial vascular disorders In L M Zimmerman and R Levine *Surgical Physiology* Philadelphia Saunders in press)

Upper Extremity The main source of preganglionic fibers which control sympathetic activity of the vessels in the upper extremity is the third to the sixth or seventh thoracic levels inclusive[10] with the possibility that the second may also contribute such neurones However there is some question as to the role that the first thoracic root plays in this regard Clinically it appears to have little significance as judged by the fact that the white communicating ramus running in it is generally left intact in the process of sympathectomizing the upper extremity and still the desired effect is accomplished On the other hand studies indicate that in the monkey and cat the first thoracic nerve possesses sympathetic fibers which are implicated in vasomotor control of the forelimb[97]

rami containing the postganglionic fibers leave the ganglionic chain primarily at the level of the first thoracic and inferior cervical ganglia the latter two structures frequently being fused to form the stellate ganglion Occasionally postganglionic fibers also arise from the third thoracic ganglion All of them then enter mainly the lower trunk of the brachial plexus and reach the arterial and venous systems of the upper extremity via the median ulnar and to a lesser extent radial and musculocutaneous nerves and their branches The vasomotor fibers are segmentally distributed in a manner similar to the sensory innervation of the overlying skin As they approach the surface of the limb they become much more numerous with the greatest number ending in the vicinity of superficial vessels

In contrast with the rest of the arterial tree in the upper extremity the subclavian artery, except possibly in its lower third is not innervated by sympathetic fibers running in the brachial plexus Instead the proximal portion receives twigs which arise directly either from the stellate ganglion from the ansa subclavia or occasionally from the vertebral ganglion The fibers from the stellate ganglion may extend the full length of the subclavian artery Although these sympathetic twigs are incapable of affecting the state of tonus of the smaller arteries and arterioles in the upper extremity by producing spasm of the subclavian artery they can still markedly reduce blood flow locally

The remaining large vessels in the upper limb for the most part receive their sympathetic innervation from fibers running in the brachial plexus The axillary artery is supplied by filaments arising from all three cords of the brachial plexus but mainly from the medial segment The lower third of the vessel may receive an additional sympathetic innervation from the median nerve The latter is the predominant source of vasomotor fibers for the brachial artery and its branches Besides this supply the brachial artery may on occasion also receive twigs from the musculocutaneous nerve the radial artery from the radial nerve and the ulnar artery from the ulnar nerve

Lower Extremity The main source of sympathetic innervation of the blood vessels of the lower extremity is through preganglionic fibers which leave the cord in the anterior roots of the tenth thoracic to the third lumbar pass through the first and second lumbar paravertebral ganglia without making synapse and terminate in the lower lumbar and upper sacral ganglia * From the latter structures arise postganglionic fibers which join the somatic nerves by way of gray communicating rami and are distributed to the peripheral blood vessels in the same manner as are the fibers of the upper extremity Most of the vasomotor nerves for the leg and foot are carried in the sciatic nerve

The femoral artery receives its sympathetic innervation from several sources One consists of nervous filaments which arise in lumbar splanchnic and genitofemoral nerves and reach the vessel by running in the adventitia of the ...

* The fact that ...
in the upp...
sur[g]ical re...
sacrificing ...

aorta and common and external iliac arteries * Another supply is from the femoral nerve and its muscular, cutaneous, and saphenous branches

The subdivisions of the femoral artery also have several sources for sympathetic innervation The proximal portion of the popliteal artery receives filaments from the posterior division of the obturator nerve and the saphenous branch of the femoral nerve The remaining part is supplied by fibers from the medial popliteal nerve The main vasomotor source for the posterior tibial and peroneal arteries is the posterior tibial nerve while that for the anterior tibial and dorsalis pedis arteries is the anterior tibial nerve

NORMAL VASOMOTOR TONUS

Factors Involved in Maintenance of Vasomotor Control

Normally, all components of the peripheral vascular system are in a state of tonus or partial contraction of the muscular elements in the vessel wall which is dependent upon the integrity of the sympathetic nervous system Of great importance in this function are the vasomotor centers in the medulla

According to most authorities, nerve impulses arising in the vasomotor centers pass down the cord and then leave it over the preganglionic fibers to cause stimulation of the postganglionic cells, not directly, but through the mediation of acetylcholine released at the synapse The impulses initiated in the postganglionic fibers then reach the effector organ in the blood vessel wall, to liberate another chemical mediator sympathin E This combines with a local receptor substance to cause partial contraction of the muscle layer of the blood vessel Recent evidence appears to support the view that sympathin E resembles norepinephrine more closely than it does epinephrine[1] The different neurohormones are believed to act by diffusing across the intervening gap in the synapse and perhaps producing momentary changes in surface potential

Variations in Normal Vasomotor Tonus

Differences in the Upper and Lower Extremities Vasomotor tonus is not distributed equally to the vessels in the upper and lower extremities For example, anesthetization of sympathetic nerves is followed by a rise of skin temperature in the foot that is of greater magnitude than that in the hand thus indicating that normally the state of tonus in the lower limb is more marked than in the upper In line with this is the finding that indirect vasodilatation (p 457) which depends upon inhibition of vasomotor tonus is much more readily accomplished in the hand than in the foot Moreover the vessels of the toes are more susceptible to constrictor influences than are those of the fingers while at the same time being relatively refractory to most medical vasodilating agents The greater sympathetic control of the vessels in the lower extremities may be related to the fact that on

* The existence of a network of sympathetic fibers surrounding the femoral artery forms the basis for the periarterial sympathectomy of Leriche However it must be emphasized that stripping the adventitia of this vessel in no way affects sympathetic control of the small arteries in the lower extremity

the assumption of the upright position a relatively greater load is placed upon them than upon the vascular tree in the upper extremities

Differences in Distal and Proximal Portions of a Limb Besides the differences already enumerated evidence has accumulated recently, chiefly through the use of a segment type of venous occlusion plethysmograph,[1] to indicate that vasomotor control is for the most part limited to the vessels of the distal portions of the extremities the hands and feet * In support of this view is the observation that under physiologic conditions spontaneous alterations in limb volume are present in the hand and to a lesser extent in the foot but not in the forearm and leg These changes appear to be the result of variations in venous tonus[3] and are abolished by sympathetic denervation The use of various types of vasoconstricting stimuli brings out other differences For example smoking[5] and the application of a pinch to the skin of the body produce a marked decrease in blood flow in the hand and foot and little or no change in the forearm Hyperventilation[7] general anoxia resulting from the inhalation of a 10 per cent oxygen mixture[4] a mental problem in arithmetic[2] and small and large quantities of epinephrine[3, 6] elicit a reduction in circulation in the hand but at the same time there is an increase in the forearm or leg Inhalation of 7 per cent carbon dioxide likewise causes a decrease in blood flow in the hand There may be either no change or an increase in the forearm and leg depending upon whether or not a systemic effect is elicited[7] The vasoconstricting response in the hand is abolished by sympathectomy[10]

The results with various medications and procedures which inhibit vasomotor control are likewise in accord with the concept that the responses of the blood vessels in the distal portion of a limb are different from those in the proximal portion Of interest in this regard is the finding of an increase in blood flow in the hand and no change in the forearm and leg following oral administration of alcohol[6] Similarly Etamon[5] Hydergine[10] and indirect vasodilatation elicit a marked increase in blood flow in the foot and hand and only a slight augmentation in the forearm and leg Furthermore temporary blocking of the paravertebral sympathetic ganglia and spinal anesthesia produce a significant elevation in skin temperature of the toes but *no rise in muscle temperature* of the calf[1] Finally Priscoline induces an increase in cutaneous and subcutaneous blood flow in the leg and foot while at the same time causing a reduction in muscle circulation in the calf[11]

Opposed to the view already presented is the observation that after temporary blocking of the mixed nerves of the forearm the local blood flow increases about twofold Such evidence has been *interpreted* to indicate that temporary paralysis of the peripheral sympathetic nerves causes *release* of vasoconstrictor tone in the vessels of the skeletal muscle[9, 11]

Interpretation of Differences in Vasomotor Control in the Extremities Anatomic studies have revealed that if relatively avascular tissues like bone fat and tendons are disregarded the hand and foot can be considered to be composed primarily of skin while the forearm and leg ...

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portion of a limb are predominantly due to alterations in cutaneous circulation, while those in the proximal portion represent to a large degree variations in muscle blood flow. On the basis of the evidence already given, it then follows that the vessels in the skin, particularly of the hand and foot, are markedly under the control of the sympathetic nervous system, in contrast to those in skeletal muscles which are not affected by alterations in vasomotor tonus. Hence a state of sympathetic hypertonus should be expected to cause a considerable reduction in cutaneous circulation in the hand and foot, with a similar but less intense type of response in the skin of the forearm and leg, while muscle flow in the latter sites should remain unchanged. Conversely, removal of vasomotor control should result in a significant increase in circulation through the skin of the hand and foot, with perhaps a slight but similar type of change in the forearm and leg, and again little or no increase in blood flow through the muscles of the latter sites.

The difference in the degree of sympathetic control of blood vessels in the distal and proximal portions of the extremities can be correlated, in part, with the function attributed to these vascular beds. For example, it is generally accepted that the hand, and to a lesser extent, the foot, play an important role in the maintenance of a constant body temperature, despite variations both in environmental temperature and in the quantity of body heat produced. For this purpose a sensitive and labile mechanism is necessary to bring about rapid changes in the amount of heat required to be lost from the body during the course of a day's activity. The vasomotor centers, through the rich sympathetic nerve innervation of the cutaneous vessels of the hands and feet, provide such a readily responsive regulation.

In contrast, the circulation through the vessels deep in the muscles of the forearm and leg contributes little to the functions of heat dissipation and conservation. At the same time, however, the vascular mechanisms must be capable of varying markedly and instantaneously with changes in the metabolic needs of the tissues. In this regard it has been shown that blood flow in the forearm may rise fifteen- or twentyfold with even a moderate degree of local physical effort. Coincident with changes of such magnitude taking place in the exercising muscles, the blood flow through the skin overlying them or in nonexercising muscles elsewhere in the extremities is either reduced, as a result of shunting of blood to the active sites, not affected, or slightly increased, depending upon the amount of work.

It would appear, therefore, that the vasodilatation in exercising muscles is primarily a local response, probably elicited by the action of metabolites formed in the active tissues, although with severe effort there may also be some passive distension as a result of an increase in cardiac output. A central control of the muscle vessels, as through the vasomotor centers, would contribute little to the efficiency of the local vascular mechanism. Even the proponents of the view that there is some sympathetic vasoconstrictor tone in muscle vessels concede that the activity of the vasomotor center has no effect on the circulatory changes taking place during or after muscular work.[11] (For further discussion of changes occurring with exercise see *Vascular Responses to Walking*, Chap. XXVIII.)

Variations in Normal Tonus Noted Clinically. The state of tonus varies widely from one normal individual to another. Some people manifest a low degree of vascular tone, possessing warm, dry hands and feet which are little affected by

extremes of environmental temperature or by emotion Others have a high degree of vascular tone with cold moist hands and feet, which cool rapidly upon exposure to cold and which may cool and sweat profusely with emotion At times one may not be able to differentiate between the normal individual with high vascular tone and the patient with a true but mild vasospastic disorder A point which may contribute to this difficulty is the fact that in one person the presence of high tonus and a labile vasomotor system may cause no distress or inconvenience while the same state in another may constitute an annoying and perhaps disabling affliction

VASOSPASM

Vasospasm represents an abnormally high degree of vasomotor tonus It is characterized by cyanosis or pallor (Fig - p -8) coldness of the skin to touch a subjective sense of coldness hyperresponsiveness to a cold environment and less often pain and edema (p 463 and Figs 4- p 31- and 43 p 313) As a result of associated sympathetic stimulation of the sweat glands hyperhidrosis is generally a part of the clinical picture of vasospasm although it is not directly related to the increased tonus of the peripheral blood vessels The coldness of the skin is due to a reduction in the amount of heat brought to the surface of the body as a consequence of the decreased cutaneous blood flow The marked reactivity of the peripheral arteries to a cold environment is related to the fact that vessels subjected to increased vasomotor control usually react to any type of noxious stimulus in an exaggerated fashion

The mechanism responsible for the pain is not entirely clear There is little doubt that vasospasm itself is implicated since it produces ischemia of tissues including sensory nervous elements Furthermore on removal of vasomotor tonus, frequently the symptom is minimized or even abolished However it is necessary to point out that pain may also exist in the absence of local anoxia Such a clinical finding has led to the belief that there may be physiologically significant afferent fibers in the peripheral sympathetic nervous system stimulation of which elicits the symptom Anatomic and physiologic confirmation has been obtained for this view [9 9 4] The relief of pain following sympathetic denervation therefore, is due either to an increase in circulation to the nervous elements to blocking of afferent impulses from the vessels or to both

VASODILATATION

Although there is no question that vasoconstrictor fibers are present in the mixed peripheral nerves the existence of a comparable vasodilator mechanism has not been established In the case of most animals the evidence favors the view that there is some provision for active vasodilatation as well as active vasoconstriction [14] However the belief that the same situation exists in man[31] has been criticized [44] Furthermore no anatomic evidence has been offered for the presence of such structures

The problem of obtaining peripheral vasodilatation in man for the most part revolves around means of inhibiting or destroying vasomotor control over the

blood vessels Because of the reduced peripheral resistance offered to the flow of blood, there is an increase in local circulation This manifests itself in the form of rubor of the skin, an elevated cutaneous temperature, a *subjective sense of* warmth and, at times a burning sensation The color change is due to a more rapid movement of blood through the tissues, resulting in a greater than normal quantity of oxyhemoglobin in the subpapillary venous plexus The increased quantity of blood reaching the surface of the body permits a greater loss of heat from it to the environment, in the process of which the temperature of the cutaneous tissues is raised Finally the sensations of warmth and burning are the patient s interpretation of the elevated skin temperature and probably result from stimulation of peripheral nerve endings by the heat It is of interest, however, that burning may also be experienced either when an impaired circulation exists, as in the case of the ischemic neuritis associated with occlusive arterial vascular disorders (p 12), or in the presence of certain entities characterized by vitamin deficiencies, such as beriberi Evidently the sensation is a nonspecific response to a number of different and unrelated agents

Since removal of vasomotor control of peripheral blood vessels provides a ready therapeutic means of increasing local circulation, it appears advisable in this section to discuss the physiologic basis for methods utilized for such a purpose as well as any possible untoward effects and clinical application The various procedures accomplish their aim either by temporarily reducing the rate of formation of vasoconstrictor impulses or by temporarily or permanently destroying the continuity of the pathway of the sympathetic nervous system somewhere in its course As a result, the number of such impulses reaching the periphery is either decreased or blocked entirely thus permitting passive dilatation of the vessels and an augmentation in blood flow (For a discussion of drugs producing sympathetic blockade see *Drugs having an inhibitory action on the sympathetic nervous system,* Chap XXX)

BLOCKING OF PERIPHERAL PATHWAYS WITH LOCAL ANESTHETICS

Peripheral Nerve Blocking

Blocking of peripheral mixed nerves in the extremities with a local anesthetic causes transient paralysis of the sympathetic elements contained in these structures and, hence limited sympathetic denervation As a result vasodilatation of the cutaneous arteries arterioles and capillaries occurs The procedure has diagnostic but no therapeutic value except on occasion when pain in a gangrenous or ulcerative toe can be temporarily controlled through anesthetization of sensory fibers (For technic, see *Procedures Used Clinically for Temporary Removal of Vasomotor Tonus* Chap IV)

Stellate Ganglion Block

The most commonly employed method for sympathetic block of the upper extremity is stellate ganglion block, preferably using the anterior route [8] The effectiveness of the procedure can be evaluated by means of the sympathogalvanic reflex If inadequate sympathetic denervation occurs it is then necessary to perform a paravertebral sympathetic block of T_1 and T

The stellate ganglion corresponds to the seventh and eighth cervical ganglia in the majority of the cases fused to the first or even second thoracic ganglia It varies in length between 1 3 and 2 5 cm (½ and 1 inch) and is irregular in shape It is located posterior to but not in direct contact with the first part of the subclavian artery

A successful block of the stellate ganglion is indicated by the development within a few minutes of the signs of a Bernard Horner s syndrome—enophthalmos ptosis miosis and cessation of sweating on the side of the block At the same time the characteristic response to sympathetic denervation—a warm dry pink hand—is noted in the corresponding upper extremity The changes in both the face and hand disappear in about one half hour after onset

Clinical Application Stellate ganglion block may be of value in the treatment of such vasospastic conditions as causalgia and posttraumatic vasomotor disorders It can also be used to remove the associated vasospasm of sudden arterial occlusion of the main arteries in the upper extremity and the widespread reflex pulmonary vascular and bronchial spasm noted in pulmonary embolism

Paravertebral Sympathetic Block

Physiologic and Pharmacologic Alterations A simple means of producing temporary vasomotor denervation of a limb is to inject procaine or longer acting local anesthetics at the level of the paravertebral sympathetic ganglia in order to block the spread of vasoconstrictor impulses from the pre to the postganglionic fibers The vasodilatation is limited to the extremity being tested while no systemic circulatory response is elicited The action may last from one half to several hours depending upon the type of local anesthetic administered * If complete blocking of all the involved ganglia has been accomplished there will be a total loss of sympathetic control over the cutaneous arterioles capillaries venules and veins On the other hand the corresponding channels in voluntary muscle are little if at all affected by such a measure (For explanation see *Variations in normal vasomotor tonus* in this chapter)

The signs of a successful block are present in approximately 15 to 30 minutes after the injection of the anesthetic In the upper extremity they are similar to those already described for a stellate block In the lower extremity there are an increase in skin temperature of the toes rubor of the foot and anhidrosis Associated with inhibition of vasomotor tone a partial anesthesia of the skin may be noted which is limited to the distribution of the genitofemoral anterior femoral and lateral femoral cutaneous nerves With procaine the changes observed in the extremities generally persist for about 30 minutes

Since with a paravertebral sympathetic block the action of the anesthetic is exclusively on the ganglia the neuroeffector organ and the muscular coat of the blood vessels continue to be reactive to various types of stimuli For example circulatory vasopressor substances like norepinephrine epinephrine or other adrenergic drugs will still cause vasoconstriction in the limb under study Pituitrin and the local application of cold will produce a similar response but through a direct action on the vessel wall On the other hand exposure of the rest of the

* The substitution of phenol 6% may prolong the block for as long as 2 to 3 weeks

body to cold will no longer have any effect on the arterial tree in the limb since anesthetization of the paravertebral sympathetic ganglia produces a block in the efferent arm of the arc essential for reflex vasoconstriction.

There are certain vasodilating measures which are still capable of enhancing the augmentation in local circulation produced by a paravertebral sympathetic block. Among these are nitrites, papaverine and the local application of heat, all of which have a direct relaxing influence on the muscular coat of the vessel. In contrast, warming of distant portions of the body will now be ineffective in causing *indirect vasodilatation in the limb* since the latter reflex is mediated through inhibition of vasomotor tonus which in the presence of a paravertebral sympathetic block already exists. Hence no further response can be expected.

Untoward Effects. A serious objection to repeated paravertebral sympathetic blocks which has recently been raised is that such a procedure may cause severe retroperitoneal hemorrhage in the patient on anticoagulant therapy and hence should not be performed under these circumstances.[17, 24, 31] If this contraindication can be supported by further reports, it will markedly limit the therapeutic application of the method. For, in two conditions in which it has had extensive clinical trial, acute arterial embolism and acute deep thrombophlebitis, there is an unquestioned *indication for the administration of anticoagulants to prevent the propagation of the clot*. It is necessary to point out, however, that the above view is not universally held.[35]

Clinical Application. Paravertebral sympathetic blocks have been used in peripheral vascular diseases for both diagnostic and therapeutic purposes. Primarily the procedure is of value in determining the degree of vasospasm or normal tonus in a limb, and hence it is used in differentiating purely vasospastic arterial disorders from organic diseases with or without associated hypertonus. It is also a necessary preliminary step to sympathectomy since the resulting changes are similar to those that would follow permanent denervation. (See *Complications of sympathectomy in this chapter.*)

As therapy, paravertebral sympathetic block has been given a clinical trial in those disorders in which vasospasm plays an important role. On this basis it has been used in causalgia, posttraumatic vasomotor disorders and in the early stage of acute arterial embolism and deep thrombophlebitis. With regard to the latter two conditions, the possible dangers of such a therapeutic approach have been stressed above. A serious objection to the therapeutic use of procaine paravertebral sympathetic blocks is that the paralysis of sympathetic activity is *transient*. Hence a prolonged effect can only be accomplished by means of repeated injections, each being associated with a certain amount of discomfort or pain to the patient.

Continuous Blockade of Paravertebral Sympathetic Ganglia

Because of the disadvantages of paravertebral sympathetic block, attempts have been made to substitute longer acting measures. Among these are continuous paravertebral procaine block,[13, 41] prolonged spinal anesthesia,[39, 43] and the introduction of local anesthetics into the epidural space using the caudal or the interspinous route.[36, 37]

The blocking action of spinal anesthesia and caudal anesthesia is on the preganglionic fibers to the lower extremities as they arise from the cord in the anterior roots and run in the white communicating rami to reach the paravertebral sympathetic ganglia The procedures generally produce complete sympathetic denervation of the arterial tree in the legs and feet Since the neuroeffector cells in the blood vessel wall are unaffected their responses to various types of physical and chemical stimuli are similar to those enumerated in the case of a paravertebral sympathetic block Besides inhibition of sympathetic vasoconstrictor impulses spinal anesthesia also causes paralysis of voluntary muscles and loss of sensation

Clinical Application Measures which produce continuous blockade of peripheral sympathetic fibers or ganglia are primarily of value during the initial stage of acute arterial embolism and deep thrombophlebitis when a marked degree of associated vasospasm is generally present They are also useful early in causalgia and posttraumatic vasomotor disorders since by reducing or even eliminating pain they permit the application of physical therapy in the rehabilitation of the patient They have a definite advantage over repeated paravertebral sympathetic blocks since they can be used in conjunction with anticoagulants without any increased risk All that is necessary is to institute them prior to the administration of anticoagulants

SYMPATHECTOMY

Theoretically sympathetic denervation of a limb through ganglionectomy appears to be based on sound physiologic principles By such a means it is possible to confine *the release of* vasoconstrictor tonus to the limb in need of a greater local circulation while vasomotor control over the rest of the body is not affected Consequently the undesirable drop in blood pressure which follows extensive sympathetic denervation as through the use of orally or parenterally administered sympathetic blocking agents is avoided Other factors which must be considered in the full evaluation of the operation are (1) whether the duration of the increased circulation is temporary or permanent and (2) whether the local changes resulting from inhibition of vasomotor tonus are at the same time beneficial or detrimental to the organism as a whole Furthermore one should be aware of the limitations and complications of sympathectomy All these points are discussed below

Return of Local Tonus

Although there is no question that sympathectomy is followed by an increase in circulation to the denervated limb the available physiologic evidence indicates that this change does not persist

Studies of Local Circulation Following Sympathectomy That there is a return of intrinsic tonus is supported by blood flow studies using the venous occlusion plethysmographic method In the normal hand the operation produces an eight fold or greater increase in circulation which is observed almost immediately after the procedure[4] However the readings soon begin to fall so that on the sixth postoperative day they are only double the preoperative rate This trend continues

to be observed on subsequent examinations The results in the feet are similar to those in the hands, except that the maximal increase in flow generally does not occur until two days after operation Several months later the rate is approximately twice that of the control level No real differences are noted between the results obtained with pre or postganglionic sections Despite the rapid reduction in blood flow, the skin temperature of the toes persists at a high level a finding which may be related to the fact that heat loss is reduced because of anhidrosis In the forearm the regain of tonus is more rapid than in the hand and foot with the result that blood flow which is at first doubled, decreases to the preoperative level in approximately four days[18] Whether the initial change in the forearm is the result of an increased circulation through the cutaneous or muscle vessels or whether it represents a composite effect in both vascular beds has not been definitely established

Basis for Return of Tonus A number of theories have been offered to explain the regain of vascular tonus which follows sympathectomy It is generally accepted that after section of a nerve, the distal portion undergoes wallerian degeneration which extends to the effector organ, and as a consequence the involved tissues manifest an increased sensitivity to chemical stimulation It is possible therefore that following sympathectomy such a change occurs in the neuroeffector cells in the blood vessel wall the chemical agent being circulating epinephrine[7, 20] or some unknown hormone[7, 30] It has also been suggested that alterations are produced in the intrinsic properties of smooth muscle of the blood vessel itself which lead to a return of tonus[10]

Another possibility is regeneration of sympathetic nerves a tendency which such tissue appears to have As a result, new pathways may develop over which vasoconstrictor impulses can reach the peripheral blood vessels Or the gap in the course of the nerve produced surgically may be bridged by rapidly growing sympathetic nervous fibers even in the presence of intervening muscle

Associated Results of Operation

Besides the increase in local circulation sympathectomy may produce several other responses Some of these may be considered beneficial and so enhance the value of the procedure while others detract from it

Effect on General Economy of Body The operation may or may not have systemic repercussions depending upon the size of the vascular bed denervated If the procedure is limited to one or two extremities it is questionable as to whether distant circulatory readjustments will result However if all four limbs are sympathectomized embarrassment of the temperature regulating mechanism may occur as a consequence of the associated widespread anhidrosis (p 456) Moreover, since the local circulation in the denervated extremities is now fixed the body is no longer capable of mobilizing the large vascular beds in these sites for the purpose of heat conservation or dissipation

Local Changes It has already been pointed out that reflex vasoconstriction and indirect vasodilatation, produced by various extrinsic and intrinsic stimuli are not observed in the denervated limb Furthermore the direct effect of cold is

now much less potent in reducing local blood flow At the same time, vaso constriction in the lower extremities associated with the assumption of the upright position[3] is eliminated Finally since a fully sympathectomized limb does not sweat the heat which would be lost through evaporation is conserved The fa t then that a more constant circulation exists during the course of the day's activity is an advantage in the maintenance of an adequate level of nutrition in the limb particularly if the blood flow is already precarious

Because of the lack of response of denervated blood vessels to certain stimuli and chemical agents a number of precautions must be taken in the treatment of a sympathectomized extremity For example indirect vasodilatation through body heating should not be utilized since such a procedure may actually produce a decrease in local blood flow This type of change can be explained on the basis that the resulting release of vasomotor tonus in the normal limbs acts to set up vascular beds of lowered peripheral resistance and as a consequence blood is shunted into the latter at the expense of the circulation to the sympathectomized limb A hot climate by eliciting vasodilatation predominantly in the normally innervated vessels may have a similar effect Parenterally administered ganglionic blocking agents like Etamon and hexamethonium are also contraindicated *because they* produce widespread sympathetic denervation but without altering the caliber of vessels in the sympathectomized limb The fact that such responses may occur is of more than academic interest particularly when dealing with an extremity with a precarious circulation

Limitations of Operation

Sympathectomy can be expected to augment local circulation only under certa n conditions The first is that the vessels must originally have been innervated by the sympathetic *nervous system In* view of the evidence presented (p 44-) this would limit the therapeutic use of sympathectomy to those conditions in which the cutaneous blood flow is at fault while there would be no basis for such a procedure if the vascular impairment is in the muscles alone Second the

the sympathetic

presence of a

almost complete occlusion little augmentation in circulation should be anticipated In the case of the cutaneous vessels not affected by an organic disease and the new collateral channels which have formed in response to the stimulus of anoxia removal of normal vasomotor tonus should produce a definite increa e in local *circulation If* vaso pasm exists this change should be even greater The claims that sympathectomy accelerates the rate of growth of collateral vessels while slowing the progress of the occlusive arterial vascular disorder have no clear-cut experimental or clinical basis

Complications

Increased Sensitivity of Denervated Vessels Besides the regain of tonus following sympathectomy in some instances there may be an actual hypertonus with the result that local blood flow now falls below the preoperative *level* Although

present with both types of surgical approaches, it is probably more often observed after postganglionic section For the most part, it is a complication of thoracic sympathectomy and rarely, of lumbar sympathectomy

Gangrene Precipitated by Sympathectomy Among the more serious complications of the procedure is the occasional appearance of gangrene shortly after operation [8] This may occur if a widespread but variable degree of organic involvement of the vessels exists locally Under such circumstances, when vasodilatation results, the blood, following the pathway of least resistance is diverted from those arteries which are almost completely occluded into the ones with less involvement, since the latter are much more capable of increasing the size of their lumen on elimination of sympathetic control As a result, there is a further decrease in circulation to the tissues supplied by the vessels with the more advanced process, thus precipitating actual gangrene Another explanation is that paralysis of sympathetic innervation causes marked dilatation of arteriovenous shunts in the relatively uninvolved digits and a rapid flow of blood through them at the expense of tissues in a latent state of gangrene To minimize the possibility of an untoward result, therefore it should be a routine step to precede all sympathectomies for the treatment of arteriosclerosis obliterans and thromboangiitis obliterans with a study of skin temperature changes produced by a paravertebral sympathetic block A decrease or no alteration in the readings for a toe or toes should be sufficient evidence on which to decide against the use of the operation

Minor Complications There are several other complications of sympathectomy that are of relatively minor consequence Among these is the neuralgia which occurs 10–14 days after operation In most instances it gradually disappears but in some it may persist for years and become resistant to therapy The symptoms may be experienced on the lateral aspect of the thigh, in the distribution of the lateral femoral cutaneous nerve (*meralgia paresthetica*) Another undesirable effect which is noted in males if both first lumbar paravertebral sympathetic ganglia are removed is difficulty in ejaculation The dryness of the skin of the sympathectomized limb can also be considered an untoward response, frequently requiring daily use of an oily medication for a prolonged period

Clinical Application

As has been indicated in several other sections of this volume sympathectomy has a limited but definite use as therapy in peripheral vascular disorders It is of value in certain vasospastic states, such as causalgia and posttraumatic vasomotor disorders, in which it is postulated that a reflex arc exists including the sympathetic nerves as its efferent limb Where vasospasm dominates the clinical picture of a disease one would also expect denervation to produce considerable alleviation of symptoms This is supported by the beneficial effects noted in Raynaud s disease in which the spasm of the digital arteries is reduced or even eliminated by the operation However, such a procedure is indicated only when the attacks are very frequent and incapacitating or trophic disturbances are present which are resistant to conservative therapy

The role of sympathectomy as a therapeutic tool in organic vascular disorders is much more limited It should not be used in the treatment of intermittent claudication alone, nor has clear-out evidence been advanced to indicate that the procedure is effective in preventing the appearance of trophic changes As therapy for ulcers or gangrene and as a preliminary step to amputation it may be a useful measure

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CHAPTER

XXVIII VARIATIONS IN CIRCULATION IN THE EXTREMITIES UNDER DIFFERENT PHYSIOLOGIC AND PATHOLOGIC STATES

VASCULAR RESPONSES TO WALKING

Physiologic Mechanisms

An understanding of the scope and extent of the cardiovascular responses to walking is essential in the proper evaluation of the pathogenesis of intermittent claudication Normally, both systemic and local mechanisms come into play with the onset of physical activity

Systemic Responses One of the first changes that occurs with exercise is an increase in venous return to the heart This is effected primarily by the pumping contractions of the active skeletal muscles, although the respiratory movements, particularly those of the diaphragm also play a role Other mechanisms are compensatory vasoconstriction in inactive vascular beds such as in the splanchnic region and the skin, and the opening of many capillaries in the exercising muscles which allows for a faster circulation through these tissues and a more rapid venous return

In order to cope with the greater quantity of blood entering the heart several regulatory factors come into play The first is a rise in pulse rate, which occurs at once or even before the physical activity is begun and is probably due to inhibition of vagal tone through the mediation of nervous impulses arising in higher centers This is followed by a more gradual secondary rise which results from stretching of the muscle fibers in the wall of the right atrium by the augmented venous return (*Bainbridge reflex*)

Aside from changes in pulse rate, the larger volume of blood entering the heart also elicits an increase in the amount ejected with each cardiac systole (*stroke volume*) The magnitude of the change is limited by the extent to which the heart can dilate during diastole, which is fixed by the pericardium As a result of the alterations in pulse rate and stroke volume the cardiac output rises With moderate exercise it may double while with heavy muscular work it may increase to as much as five or six times the resting level[4]

Local Vascular Changes With the onset of exercise there is a marked augmentation of circulation through the active muscles This is the result not only of a greater quantity of blood reaching them per unit of time due to an increased cardiac output, but also of dilatation of blood vessels locally The elevated blood flow persists during the period of exercise and for some time after return to the resting state The basis for the vasodilatation is not entirely clear although experimental evidence[8, 9] suggests that chemical substances are released from the exercising muscle fibers and that these are responsible for the relaxation of the vessels and the subsequent augmentation in circulation Such agents as histamine acetylcholine and adenylic compound have all been proposed as the active element That the local dilatation is due to a reduction in sympathetic control over the muscle vessels is doubtful since such an innervation if it exists at all is minimal (For further discussion see *Variations in Normal Vasomotor Tonus* Chap XXVII)

Aside from the increase in local blood flow another mechanism which is called into play to supply the markedly elevated metabolic needs of the active tissues is a greater utilization of the oxygen present in the blood Whereas under resting conditions the venous blood ordinarily demonstrates approximately 75 per cent oxygen saturation, with exercise the portion which has passed through active muscles may have only as little as 20–30 per cent This increase in the coefficient of utilization is brought about by a displacement of the oxygen dissociation curve to the right as a result of an augmentation in carbon dioxide uptake and in the case of severe exercise of the production of acidosis Another factor which favors the rate of oxygen diffusion from the blood is the significant increase in the number and size of the open capillaries in exercising muscles

INTERMITTENT CLAUDICATION

In occlusive arterial vascular disorders affecting the arteries to the muscles the ability of these vessels to dilate during periods of physical stress is markedly impaired as a result of the local inflammatory or degenerative process Hence the metabolic needs of the active tissues are not satisfied instantaneously and fully, and as a consequence pain is produced (For discussion of clinical aspects of this state see *Intermittent Claudication* Chap I)

The immediate factors responsible for the appearance of intermittent claudication have not been established although it is generally accepted that ischemia is the underlying cause The possibility has been offered that in the presence of the latter state some stable chemical or physiochemical agent (*factor p*) is liberated within the mass of exercising muscles This substance accumulates in the tissue spaces increasing in amount with each muscular contraction until eventually its concentration rises to a point at which stimulation of the local nerve endings occurs[1, 18] With cessation of physical activity there is a rapid return of the metabolic needs to a resting level, so that now the impaired arterial circulation is adequate for tissue requirements As a result no further accumulation of pain producing factor takes place while the quantity which has been formed during exercise either diffuses into the blood stream or is destroyed locally With a lowering of the concentration of the material the nerve endings are no longer

stimulated The duration of symptoms will depend upon the size of the "blood flow debt" incurred during the period of exercise and the efficiency of the local compensatory mechanisms to cope with it subsequently

VASCULAR RESPONSES TO CHANGES IN ENVIRONMENTAL TEMPERATURE

Role of the Extremities in Heat Dissipation and Conservation

Before describing the vascular alterations elicited by exposure to different environmental temperatures, it is necessary to discuss the role of the extremities in the maintenance of a normal body temperature Since the four limbs constitute about 65 per cent of the body surface, it is obvious that the rate of cutaneous blood flow through them would be a potent factor in the conservation or dissipation of body heat and hence in body temperature regulation However, considerable evidence has accumulated recently to indicate that not all portions of the extremities are equally important in this function When the need for heat dissipation is moderate then vasodilatation will occur only in the hands which possess relatively large numbers of arteriovenous shunts Later, the vessels in the feet will be called into play Only if body heating is more intense or heat production is markedly increased does vasodilatation take place in the skin of the proximal portions of the limbs, the forearms and legs When body heat must be conserved again, the part played by the blood vessels in the hands and feet is much greater than that of the vessels elsewhere in the extremities The arteries arterioles, and especially the arteriovenous shunts constrict thus markedly reducing the rate of cutaneous blood flow in this fashion body heat is conserved If the need is very great then the vessels in the forearms and legs also become involved in this reaction

Role of the Sympathetic Nervous System in the Maintenance of a Constant Body Temperature

Normally Innervated Limb The finding that the hand and foot are primarily involved in the role of heat conservation and dissipation can be correlated with the richness of the sympathetic innervation of the vessels in these vascular beds All the experimental evidence indicates that increased circulation through the distal portions of the extremities permitting more effective heat dissipation, is accomplished by inhibition of vasomotor tonus to the blood vessels Reduced blood flow and conservation of body heat result from a rise in vasomotor tonus and a consequent greater constriction of the vessels

Sympathectomized Limb When sympathetic denervation of an extremity is accomplished the local vascular beds no longer contribute significantly to the function of heat dissipation or conservation The circulation remains constantly high and is not influenced by changes in body temperature At the same time the normal mechanism of loss of heat through evaporation of sweat is eliminated since the sweat glands are not active in a sympathectomized limb This point must be kept in mind when contemplating sympathectomy especially of all four

extremities Under the latter circumstances if the need for heat dissipation is increased as in a warm environment sweating may become quite marked in such sites as the back and the anterior abdominal wall where ordinarily this function is minimal Such a response can become a source of great discomfort during the summer months particularly to the female patient since it requires frequent changes of clothes Furthermore this new mechanism is generally not as efficient as the one involving the hands and feet, and hence in a very hot environment there may actually be a rise in body temperature

Exposure to Local Heat

Exposure of a limb to heat produces maximal dilatation of cutaneous and subcutaneous arteries arterioles, capillaries, venules and veins The question of how much dilatation of muscle vessels occurs has not been fully answered, but there is little doubt that at least the ones just below the subcutaneous tissues are affected The action of heat is directly on the blood vessel and is not dependent upon the integrity of the sympathetic nervous system In fact this agent will elicit a further increase in blood flow in the sympathectomized limb

Clinical Application Despite the potent vasodilating effect of heat its use in arterial peripheral vascular disorders is definitely contraindicated a view which has been repeatedly stressed in the text First exposing a limb with an impaired arterial circulation to such an agent raises the local metabolism of the tissues to a level greater than that capable of being taken care of by the ensuing increase in blood flow This is due to the presence of inefficient compensatory circulatory mechanisms The discrepancy between these factors results in a relative anoxia of tissue and thus predisposes toward nutritional disturbances

The second point involves the cooling effect of circulating blood Ordinarily when heat is applied to an extremity with a normal circulation the blood passing through the cutaneous vessels actually lowers the temperature of the part Hence the tendency to cause a burn of the skin if the heat is sufficiently intense to produce such a response is decreased However in the presence of an impaired blood supply the effectiveness of this mechanism is reduced and therefore the almost full effect of the heat is allowed to act upon poorly nourished skin Consequently a burn may follow which almost invariably results in the formation of ulceration and gangrene or if nutritional disturbances already exist the heat may cause their rapid extension

In the case of thrombosis of superficial or deep veins of the extremities local heat can be used as treatment with impunity provided reliable tests have demonstrated a normal arterial circulation In the presence of deep thrombophlebitis of either the lower or upper extremities the procedure is of value if there are signs of associated sympathetic hypertonus such as coldness cyanosis and hyperhidrosis

Body Heating Producing Indirect or Reflex Vasodilatation

Application of heat to distant portions of the body will produce vasodilatation and increased blood flow locally in the limb The change is due either to stimulation of temperature regulating centers in the brain by the heat carried internally through the venous blood from the warmed portions[7] or to the initiation of af

ferent impulses in the heated skin [12] In any event, there follows a decrease in the number of vasoconstricting impulses arising in the vasomotor centers, and, as a consequence, passive dilatation of the cutaneous blood vessels in the limbs The augmented blood flow through the superficial veins permits a greater loss of heat from the blood to the environment and hence a more rapid dissipation of body heat The response is dependent upon the integrity of the sympathetic nervous system and is not noted in the sympathectomized extremity

Clinical Application It has already been pointed out that indirect vasodilatation is of value clinically both as a diagnostic and a therapeutic procedure Besides giving information regarding the status of existing vasomotor tonus, it affords a means of increasing cutaneous blood flow without producing a corresponding rise in metabolic requirements of the tissues (p 203) Such a response is in contrast with the change produced by the direct application of heat (For technic of producing indirect vasodilatation see *Procedures Used Clinically for Temporary Removal of Vasomotor Tonus,* Chap IV)

Exposure to Local Cold

Local cold is a potent vasoconstricting stimulus It has an effect on all arterial and venous elements except the capillaries and venules which dilate passively [8] The resulting stasis, particularly of the minute cutaneous vessels, is responsible for the cyanosis of the skin associated with exposure to cold With continued application flushing may take place as a result of the initiation of an axone reflex which causes active vasodilatation of vessels locally (p 414) Apparently the stimulus of cold induces a minor degree of injury, which in turn is responsible for this vascular reaction The resulting increase in cutaneous blood flow can be considered in the light of a protective mechanism against the deleterious effects of the noxious agent [16]

Clinical Application Since cold causes vasoconstriction it is clear why an extremity with an impaired arterial circulation should be protected from such an agent In the presence of both structural changes and vasospasm the response will further accentuate the tissue ischemia Even in the sympathectomized limb local application of cold will cause vasoconstriction However the degree of reduction of blood flow with the same intensity of stimulus will be less than before operation, while the drop in temperature necessary to induce an attack of vasospasm must now be greater Such alterations in response are the basis for the use of sympathectomy in Raynaud s disease

Cold as a therapeutic agent has a very limited value in peripheral vascular disorders It is true that this stimulus does cause a reduction in the metabolic needs of the exposed tissues, and hence theoretically it would appear to be indicated in conditions in which there is a marked impairment in local circulation such as in sudden occlusion of a main artery by an embolus Actually, however the vasoconstricting effect of the cold far overshadows any beneficial effect that might result from a lowering of the metabolic requirements For similar reasons the use of contrast baths, i e, alternately immersing the limb in cold and hot water plays no significant role as therapy Frequently the patient with an occlusive arterial vascular disorder will experience pain with both types of stimuli At the same time,

it is questionable as to whether any increase in cutaneous blood flow will result from the procedure Finally local cold has been used in deep thrombophlebitis but with only occasional advantage

Exposure to Body Cooling

Application of cold to distant portions of the body will produce vasoconstriction of the cutaneous blood vessels in the extremities This response is dependent upon the integrity of the sympathetic nervous system The explanation for the change is probably two fold First cold applied to skin acts as a strong noxious sensory stimulus which causes reflex vasoconstriction Second the blood passing through the sites exposed to this agent is cooled so that when it enters the interior of the body and is circulated through the temperature regulating centers the latter are affected As a result, the number of vasoconstricting impulses arising in the vasomotor centers is increased thus causing construction of the cutaneous blood [illegible] Consequently peripheral blood [illegible]

Clinical Implications From the foregoing it can be seen why the patient with an impaired cutaneous circulation in the extremities should be protected not only from local cold but also from the deleterious effect resulting from exposure of the rest of the body to this stimulus On the other hand the blood vessels in a sympathectomized limb are no longer affected by cold applied to distant portions of the body This loss of reflex vasoconstriction is a desirable state and constitutes one of the therapeutic advantages of the operation

FACTORS INVOLVED IN THE NORMAL INTERCHANGE OF FLUIDS

Before discussing the physiologic and pathologic alterations responsible for edema it is necessary first to review briefly the mechanisms which are concerned in the normal movement of fluid across the capillary barrier

Capillary Blood Pressure One of the most important factors which determines the rate of interchange of fluids at the level of the capillary is the blood pressure or filtration pressure in this vessel It represents the portion left of the energy contributed to the blood by the contraction of the left ventric[illegible] been dis[illegible]

a [illegible]

tl [illegible]

a [illegible] have revealed that at the a[illegible] end of the vessel the average pressure is 32 mm Hg while at the venous portion it has fallen to 12 mm Hg[13] This gradient in pressure is of considerable significance in the control of fluid interchange

Capillary pressure can be altered by a number of different conditions some of which in extreme degrees lead to edema An increase may occur as a result of the local application of heat which produces dilatation of arterioles and a consequent augmentation in blood flow or after mechanical injury or inflammation of the skin which has a similar effect Cooling of the skin causes vasoconstriction and a sharp drop in capillary pressure followed in a few minutes by a secondary rise due to the state of reactive hyperemia which ensues[14] Finally capillary pressure

is markedly influenced by the position of an extremity In dependency there may be a rise to as high as 50 mm Hg in the arteriolar end, resulting from the additive effect of the hydrostatic pressure of the column of blood in the vessel, while on elevation the reading may fall to a level below that exerted by the osmotic resistance of the blood proteins

Osmotic Resistance of Blood Proteins This important factor in the transport of fluid across the capillary membrane is dependent upon the existence of an impermeability of the capillary wall (except in the liver and perhaps in a few other sites) to substances composed of large molecules, such as albumin, globulin, and the various formed elements of the blood As a result, a mechanism is at hand whereby fluid which could ordinarily pass out of the lumen of the vessel is prevented from doing so by the osmotic pull of these materials Such a force is relatively uniform throughout the arterial tree and is normally equivalent to 26 mm Hg The presence of small amounts of protein in the extracellular fluid may be attributed to a constant slight seepage through the capillary wall possibly with contributions from cells bathed by the fluid

At all times, therefore, a dynamic equilibrium exists between the filtration pressure in the capillary and the osmotic resistance of the blood colloids the effective filtering pressure being the difference between the two In the arteriolar portion of the vessel, the filtration pressure predominates (32 mm Hg as opposed to 26 mm Hg) and hence the direction of flow of fluid is toward the tissue spaces This results in a concentration of blood proteins in the venous end of the capillary with an increase in blood osmotic resistance Simultaneously a reduction in filtration or capillary blood pressure is taking place as the blood passes through the capillary bed With conditions thus reversed at the venular portion of the capillary there is now a movement of fluids from the tissue spaces into the blood stream

Other Factors Influencing Movement of Fluid Among these is the protein in tissue fluids which possesses a minor osmotic pull thus tending to cause a flow out of the capillary lumen, while at the same time it exerts an osmotic hold on the extravascular fluids already present However, a simultaneous rising tissue pressure, due to distension of the intercellular spaces, would have the effect of discouraging further movement of fluid out of the blood stream This factor is contributed to by the inherent inelasticity of tissues on being subjected to stretch and by less effective lymphatic drainage

In summary the normal amount of tissue fluid is largely dependent upon the quantity filtered across the capillary membrane this in turn being influenced by such factors as the magnitude of the effective filtering pressure the state of capillary permeability and the efficiency of the mechanisms responsible for the removal of fluid through venous and lymphatic channels

EDEMA

Since edema is a common finding in various types of vascular disorders it is necessary to discuss the alterations both physiologic and pathologic which lead to formation of this state (For clinical implications see *Swelling* Chap VI)

PHYSIOLOGIC EDEMA

Dependency That the body is constantly on the verge of edema is exemplified by the conditions existing in the individual who stands quietly in one position for more than 30 minutes Under such circumstances the volume of the lower extremities will increase several hundred cubic centimeters as a result of an excess filtration of fluid into the tissue spaces This type of change is due to the additive effect of hydrostatic pressure on capillary pressure There are several factors however which limit the extent and degree of such a response The first is the tissue pressure which eventually rises to a level which is greater than the augmented capillary filtration pressure Another is the contraction of voluntary muscles in the lower extremities which assists the propulsion of lymph and blood out of the limb Finally muscle tone contributes to this function

Heat An increased tendency to swelling is frequently noted in a warm or hot environment This is evidently related to the local vasodilating effect of such a stimulus on the arteries and veins producing an increase in arterial inflow and a decrease in resistance of the veins to stretching The latter response allows the venous tree to become even more distended by the greater quantity of blood entering the extremity thus accentuating venous stasis Such a change is reflected back into the capillaries as an elevated filtration pressure Another factor which may contribute to the edema is the lassitude and disinclination to move the body that follow exposure to a hot environment As a result the pumping effect of contracting muscles on the thin walled veins and lymphatics is lost and hence both venous and lymphatic stasis is produced

Adiposity The obese individual has a greater tendency to edema of the lower extremities than the thin one for several reasons First fat is a good insulator and hence when deposited in the subcutaneous tissues it reduces the dissipation of body heat by conductance As a result there must be further vasodilatation of peripheral vessels to carry out this function Another point is that the stout person may have a more placid disposition and hence does not have the motivation to move around as much such physical inactivity also leads to a higher venous pressure in the feet and a less efficient movement of blood and lymph out of the lower extremities A contributing point is the fact that replacement of fibrous subcutaneous tissue by fat offers a diminished support to the superficial veins

The stout female has an even greater tendency for edema formation especially during the summer months Of interest in this regard is the observation that women as a rule sweat less than men Therefore under conditions of equal heat production and environmental temperature greater dilatation of peripheral vessels particularly the arterioles must take place in order to maintain a heat balance This type of response leads to a higher filtration pressure in the capillary bed and an increased movement of fluid out of the lumen of the vessels into the tissue spaces

Pathologic Edema

Local Vascular Disorders

Deep Thrombophlebitis The underlying mechanism for the prominent finding of swelling in acute deep thrombophlebitis of the extremities is primarily an interference *with the movement* of blood out of the limb due to occlusion of the main venous channels As a consequence, there is a stasis in the small venules and capillaries, followed by a rise in pressure within their lumen, sometimes to a level five times as great as normal The latter change acts as an augmented capillary *filtration pressure to cause the expression of fluid from the blood stream* into the extravascular spaces At the same time it prevents the normal movement of tissue fluid into the venular portion of the capillary Because of the venous stasis there may also be some anoxia of the capillary wall, producing increased permeability which *further contributes to transudation of fluid (Fig 32, p 246)*

Interference with lymphatic drainage from the limb is also responsible for the swelling in acute deep thrombophlebitis This is considered in part to be due to an inflammation of the neighboring large lymphatic vessels accompanying the phlebitis and periphlebitis [11] The resulting lymphatic stasis is further exaggerated by the increased burden placed on the lymphatic system through the loss of the normal mechanism of removal of blood via venous channels

Another factor which is implicated in the production of lymphatic stasis is spasm of medium and small sized arteries, due to a vasomotor reflex initiated by the thrombosed segment of vein acting as a focus of irritability As a result of the reduced pulsations in the arterial tree the neighboring thin walled lymphatics are no longer subjected to the normal pumping action supplied by the rhythmic distension and recoil of the arteries with each cardiac cycle [3, 10] Hence stagnation of tissue fluids and accumulation of proteins in the perivascular spaces will occur Such a situation is conducive to edema formation since the osmotic pressure exerted by these substances prevents reabsorption of tissue fluid into the vascular tree

The vasospasm which *accompanies acute deep thrombophlebitis contributes to* the swelling through other mechanisms as well Besides the effect on lymphatic drainage, arterial spasm produces anoxia of the capillary endothelium thus causing an augmented permeability and hence transudation of fluid [0, 1] Because of *the associated venospasm* there is a further increase *in venous pressure favoring* the movement of fluid from the vascular bed into the perivascular spaces and at the same time preventing the change from occurring in the opposite direction

The edema that appears as part of the postphlebitic syndrome when the patient again becomes ambulatory (Fig 36 p 277) reflects an inefficient venous system incapable of coping with the return of blood from the lower extremity on the assumption of the upright position As a result of interference with venous outflow, there is a tendency for blood to accumulate in the veins in the distal portion of the extremity and to produce venous stasis This leads to an increase in venous pressure, which is transmitted back into the venules and capillaries as a raised filtration pressure Consequently there is a greater than normal movement of fluid through the vessel wall into the tissue spaces

If the swelling observed in the postphlebitic syndrome is left unchecked eventually it begins to lose its pitting character and to resemble lymphedema The exact mechanism responsible for the change is not clear although several views have been offered In one it is premised that as the edema fluid remains in the extracellular spaces for any period of time its protein content increases, perhaps through absorption of water The presence of such protein rich fluid eventually provokes a fibroblastic reaction which leads to local obstruction of the small lymphatic channels and lymphatic stasis Another possibility is that the main lymphatic vessels in the groin are occluded by the scarring and fibrosis which almost invariably develop in the tissues surrounding the involved segment of femoral vein

Occlusive Arterial Vascular Diseases On occasion edema may be present in an extremity with a markedly impaired arterial circulation demonstrating impending or existing nutritional disturbances (Fig 8 p 85) Such a response generally occurs after the limb has been kept in dependency for a protracted period of time in an attempt to obtain relief from the associated severe pain The swelling is evidently due to two factors first an increase in filtration pressure in the lumen of the capillaries representing the additive effect of the hydrostatic pressure operating in dependency, and second a greater permeability of the capillary wall consequent to the existing local ischemia Both mechanisms tend to cause a more rapid movement of fluid from the blood stream into the tissue spaces to produce edema

Vasospastic States Swelling may be present in vasospastic conditions as a result of mechanisms which are similar in many regards to those responsible for the edema of acute deep thrombophlebitis Among these are the reduced pumping action of the arteries on the lymphatic channels producing lymphatic stasis and anoxia of the capillary wall causing greater permeability In the case of frostbite an additional factor contributing to the state of ischemia is thrombosis of small arteries The fact that the extremity suffering from vasospasm is frequently held continuously in a dependent position may also facilitate the formation of edema mainly because of the increased hydrostatic pressure that ensues and because of the loss of the normal pumping action on the thin walled lymphatics and veins normally supplied by the contractions of voluntary muscles

Removal of vasomotor tonus through temporary or permanent sympathetic denervation will generally cause a reduction or elimination of the swelling (Fig 42B p 31-)* since this leads to a re-establishment of the mechanisms which accelerate the movement of lymph out of the limb Although it is true that at the same time there is arteriolar vasodilatation which causes an elevated capillary filtration pressure this tendency toward edema formation is more than balanced by the elimination of the increased capillary permeability through removal of the anoxic state

Local Inflammation This state is almost invariably associated with some degree of swelling Among the mechanisms responsible for such a response are vasodilating substances produced in the site of involvement and acting on the arterioles

* The fact that this occurs is the basis for the clinical use of repeated paravertebral sympathetic blocks and adrenergic blocking agents in the treatment of the edema of acute deep thrombophlebitis and of sympathectomy in the case of posttraumatic vasomotor disorders

locally to cause an augmented circulation As a consequence, there is an elevation of capillary blood pressure to heights as great as 50 mm Hg Associated with these changes is an increase in capillary permeability, which further facilitates the movement of fluid out of the blood stream into the tissue spaces The fact that at the same time protein is permitted to escape from the blood stream helps perpetuate the state of edema

Systemic Disorders

Congestive Heart Failure The edema commonly present in this condition is due to a number of complex and by no means clearly understood mechanisms Among these is a reduction in cardiac output and the resulting decrease in renal blood flow and glomerular filtration Another is salt retention, although the agents responsible for this state have not been identified Also considered as possible etiologic mechanisms are such factors as venous congestion of the kidneys and alterations in the hormonal salt and water retaining influences on tubular reabsorption The increase in central venous pressure generally noted may contribute to edema formation, since it is reflected backward as an elevated capillary filtration pressure Whether this change is the result of an inability of the right side of the heart to take care of the venous return or whether it is related to an augmentation in circulating blood volume has not been established Recently evidence has been advanced to implicate the liver in the production of edema Greater capillary permeability as a possible etiologic factor does not receive support from the finding of a low protein content in the edema fluid

Aside from the above changes, there are other factors which may contribute to the swelling of congestive heart failure First, the cardiac patient has a natural disinclination for physical exertion, and as a result of the reduction in frequency of contractions of muscles in the lower extremities there is tendency for a rise in mean venous pressure in the feet Second this type of individual may sweat less readily than a normal person Consequently, a greater degree of vasodilatation is required in the removal of body heat in order to compensate for deficient evaporation In hot weather such a change is magnified As has already been mentioned all these responses are conducive to a greater movement of fluid out of the capillary wall into the tissue spaces

Lowered Blood Protein Level In entities in which the osmotic resistance of the blood proteins is reduced because of a decrease in the quantity of circulating albumin, edema can be expected However there is no constant critical level at which this will occur Examples of such an altered mechanism are the nephrotic syndrome, in which albumin is being lost in the urine and cirrhosis of the liver and nutritional deficiencies in which there is an impairment in the production of this substance All these conditions are characterized by a movement of fluid out of the vessels into the tissue spaces because of the now relatively greater effectiveness of the capillary filtration pressure, opposed by a smaller osmotic resistance of the plasma proteins Associated with the hypoalbuminemia there may be increased amounts of antidiuretic substances present in cirrhosis which augment tubular

reabsorption of sodium and water and an absence of a renal hormone in the nephrotic syndrome which normally regulates capillary permeability

Retention of Salt A rise in the quantity of salt and water retaining hormones sufficient to produce edema may be noted in several other states Among these are hypersecretion of the adrenal glands and the continued administration of desoxycorticosterone acetate cortisone or corticotropin

SKIN COLOR

As has been discussed in Chapter II, a study of skin color in the extremities is of great value in determining whether or not impairment in local circulation exists For this reason it is necessary to have an understanding of the various factors that contribute to normal skin color and to their modification by pathologic states

Factors Responsible for Normal Skin Color

For the most part if the relatively permanent changes produced by the deposition of pigment are disregarded skin color is a *reflection of the rate of blood flow through the cutaneous vessels* Since the superficial venules form a dense meshwork in the subpapillary region they present a larger actual surface in the plane of the skin than do vessels at greater depths and hence their influence on skin color is considerable This is particularly true in the case of the relatively white skin of the trunk and limbs As the cutaneous capillaries dilate their role in skin color also increases in importance although in the hand and sole of the foot where these structures are more numerous their contribution is great even when they are not in a dilated state

Under physiologic conditions therefore with the body at rest and the skin warm the cutaneous venules and capillaries are almost completely responsible for skin color However in the presence of pallor the skin becomes more transparent thus permitting the color of deeper lying subcutaneous veins to play a part also

The tint of the skin is due chiefly to the relative amounts of reduced hemoglobin and oxyhemoglobin in the channels concerned Blood enters the minute vessels in an arterial state and leaves in a more venous state the existing tint being intermediate between the two and depending in great part upon the rate of blood flow

Mechanisms Responsible for Changes in Skin Color

Rubor This color change is produced by a number of different physiologic and pathologic states Normally a bright red arterial color indicates an increased circulation and under these circumstances the skin is warm or hot Such a response is noted when the [illegible] ture and the need [illegible] arterioles capillaries [illegible] and venules The rubor that occurs on the termination of a state of anoxia (reactive hyperemia) also represents a marked augmentation in cutaneous blood flow The appearance of transient

rubor on placing a limb in dependency may be either a normal or abnormal response the change being the result of relaxation of the subpapillary venous plexus *followed by pooling of blood* The differential point is the fact that in the presence of an impaired circulation, there is also a lowered cutaneous temperature

A bright red, somewhat cyanotic, color in a cold foot maintained in the horizontal position (Fig 2D, p 28) is an abnormal sign It may indicate that the *arteriovenous shunts* are permanently open, due to some pathologic process, and consequently the little blood that reaches the toes is diverted into the venous side of the circulation without traversing the capillaries[10] Because of the resulting higher concentration of oxyhemoglobin in this complement of venous blood there is a tendency for the skin to assume a redder hue Another possible explanation is the existence of some abnormality of the enzyme systems which prevents the removal of oxygen from the blood in its passage through the tissues

Cyanosis Such a change also has various interpretations A blue color elicited by exposure to a cold environment is generally a normal response and indicates constriction of arterioles and veins causing stasis in the capillaries and venules and hence a better opportunity for the transference of oxygen across the vessel barrier to the extracellular spaces Invariably accompanying this type of change is a lowered skin temperature

Cyanosis in the presence of a warm environment generally indicates the existence of vasospasm of the arterial tree particularly of the arterioles (Fig 2B *and C, p* 28) *The responsible mechanism is similar* to that which operates in the case of a normal limb exposed to a cold environment namely a slowing of blood flow through the minute vessels An example of this type of response is the cyanosis noted in such unrelated states as acute deep thrombophlebitis, the late stage of trench foot frostbite, immersion foot and anterior poliomyelitis rheumatoid arthritis, disuse atrophy and painful posttraumatic disorders The differentiation of cyanosis having a vasospastic basis from that due to organic structural changes in the vessels rests on its disappearance in the case of the former after removal of vasomotor tonus (*Chap IV*) (*For the explanation of* cyanosis of Raynaud's disease see *Pathogenesis* Chap VIII)

There are several other causes for cyanosis Its rapid appearance on placing the limb in dependency implies an impairment in local arterial circulation with the color change being due to the existence of large quantities of reduced hemoglobin *in the blood that remains in the toneless superficial vessels* The presence of a warm cyanotic skin in contrast with the low cutaneous temperature observed with vasospasm suggests that the responsible mechanism is some systemic abnormality, such as congenital heart disease in which venous blood is entering the general circulation or a condition in which proper oxygenation of blood is not taking place because of some pathologic process in the lungs

Pallor This type of change in a limb may have different implications depending upon the other abnormalities associated with it A coexisting normal or high cutaneous *temperature indicates that there is an adequate rate* of blood flow through the subcutaneous vessels but some constriction of the minute cutaneous channels A similar response may be noted in the presence of a marked reduction in circulating hemoglobin as the result of some type of

blood dyscrasia in which the rate of peripheral circulation is not affected or even increased A cold pale limb however, signifies a definite reduction in cutaneous blood flow, with emptying of the subpapillary venous plexus of blood Under such circumstances the pallor may be intensified by elevating the extremity this maneuver helping to drain the blood out of the limb at the same time that arterial inflow is impeded by hydrostatic pressure (*plantar pallor test*, Chap II)

ALTERATIONS IN SKIN TEMPERATURE

A number of factors are responsible for the level of cutaneous temperature under resting conditions Ordinarily it is the resultant of the heat *conveyed to the skin* by the blood and that lost to the environment through radiation convection and vaporization Since the amount of heat brought to the skin is dependent upon the rate of local blood flow surface temperature readings can be considered to be a qualitative index of the cutaneous circulation through the part under study provided the external environment remains constant and the limb is not exposed to drafts (For clinical implications of changes in skin temperature, see *Alterations in skin temperature* Chap II)

The control skin temperature level of the digits may *spread over a considerable* range Readings which are lower than the room temperature to which the extremity is exposed under average conditions (20°C 68°F) suggest *increased sympathetic* activity producing excessive perspiration and a reduced *cutaneous* circulation through marked vasoconstriction of the arteries locally As the sweat evaporates cooling of the skin to a point below the environmental temperature may ensue *Figures that* are 5 to 6 degrees above that of the room indicate a normal *state of vasomotor tonus* while those that are considerably higher imply an increased *cutaneous blood* flow due to low sympathetic activity

In the presence of an occlusive arterial vascular disorder there may be a low cutaneous *temperature but frequently* it is necessary to determine the contributing role of vasospasm in the *response* (Chap IV) before attributing the change wholly to permanent structural *disease of* the cutaneous blood vessels It is of interest that at times the apparent paradox exists of a higher skin temperature in the foot with an organic *impairment* in circulation than in the opposite either normal or less involved limb *This is probably* due to the production of a very efficient cutaneous collateral *circulation* Another important point to emphasize is the fact that minor or even *greater changes* in arterial inflow through main channels may exist without there being *a corresponding* reduction in cutaneous temperature From such findings it can therefore be *concluded* that a normal skin temperature does not necessarily rule out the presence of an impaired arterial circulation

VASCULAR RESPONSES TO LOCAL ANOXIA

The circulatory *changes* produced by local anoxia have both diagnostic and therapeutic implications since such a state is almost always present in all types of occlusive arterial vascular disorders and to a lesser degree in vasospastic conditions

Changes Occurring During Period of Anoxia

Chronic Anoxia If anoxia persists and is slowly progressive, then it can act as a potent stimulus to the growth of a collateral circulation (p 4-0) The finding in thromboangiitis obliterans and arteriosclerosis obliterans of a normal cutaneous blood flow in a limb with a totally occluded main arterial channel can be explained on this basis A comparable type of response is present in the case of a large arteriovenous fistula, since the part of the limb distal to the lesion suffers from a chronic state of anoxia

Acute Anoxia If the state of anoxia occurs suddenly and is complete and persistent, the viability of tissues is lost and irreversible changes ensue Such a situation may exist when a main arterial channel is occluded by an embolus or a thrombus and no opportunity is afforded for the establishment of an adequate collateral circulation Similarly, trauma to a main artery, necessitating ligation, or surgical removal of an arterial aneurysm may result in death of tissues, particularly in the distal portion of the limb

Changes Occurring after Reversal of Experimental Anoxia

If complete anoxia, produced by the application of an arterial occlusion pressure to a limb is eliminated by release of the compression, immediately upon the re establishment of the circulation, there is a period in which the local blood flow is increased above the control resting level This state of augmented circulation is called reactive hyperemia The exact mechanism responsible for the circulatory change is not clear, but it is generally believed that the terminal arterioles and capillaries dilate as a result of the action of slowly diffusible substances accumulated in the extravascular fluids during the period of arterial arrest [17] It has also been suggested that these agents are similar to histamine

The reaction forms a means whereby the local needs of tissues temporarily made ischemic are quickly satisfied This type of change is observed in the case of continuous application of pressure to the body where it comes in contact with its support, as in the sitting position Such a situation, if prolonged results in a reduction in arterial inflow to the compressed parts and eventually discomfort This then leads to a change in position of the body so as to remove pressure from the involved portions As a result these areas are flooded by blood and restored to their previous normal state [17] Another example of the elicitation of reactive hyperemia is noted following the release of digital spasm in Raynaud's disease Finally, the same type of change occurs after the continuous exposure of the skin to cold Although at first vasoconstriction of cutaneous blood vessels and pallor follow such a stimulus these changes may then be replaced by temporary vasodilatation and rubor

It has been found that the excess blood flowing into the limb during the period of reactive hyperemia grossly approximates the amount that would have entered if the arterial occlusion pressure had not been applied [1, 5] On the basis of such results, the use of intermittent applications of high pressures to a limb with an impaired arterial circulation would appear to have no therapeutic value since the transient increase in circulation merely repays a blood flow debt incurred

previously Actually such a procedure is contraindicated inasmuch as the production of a complete state of anoxia even though for only a short time is inadvisable in a limb already in a precarious state

Repeated applications of venous occlusion pressures as obtained with the intermittent venous occlusion machine (Chap XII) are also ineffective but for different reasons Under these circumstances there is no significant interference with arterial inflow and hence no production of an oxygen debt or a state of anoxia Therefore the removal of the venous occlusion pressure is not followed by any increase in local circulation

Besides the use of such procedures as the venous occlusion plethysmographic method for demonstrating the total increase in blood flow during the period of reactive hyperemia the alterations in skin color can be considered to represent a qualitative index of the changes occurring in the cutaneous circulation For this reason they have been used as the basis for a clinical test of circulatory efficiency (See *Reactive Hyperemia Test* Chap II)

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CHAPTER

XXIX INTRAVASCULAR BLOOD CLOTTING AND ITS PREVENTION

INTRAVASCULAR THROMBOSIS

Logically it would appear necessary to preface a presentation of the subject of intravascular thrombosis with a discussion of the factors responsible for normal blood clotting However an attempt to obtain a clear concept of this subject through perusal of the current literature leaves the average reader in a state of bewilderment That there are so many conflicting views in this field is probably an inevitable consequence of the fact that the fundamental problems involved are not fully understood Therefore to present one or several of the existing hypotheses in a volume of this sort would be without meaning since none has acquired sufficient permanency and acceptance to warrant such a step However if first hand information is desired regarding the ramifications and intricacies of this subject reference can be made to the papers of authors who are proponent of the different views [1 2 21 2 26 37 38]

Factors Responsible for Venous Thrombosis

Under certain circumstances the efficiency of the various factors which maintain the fluidity of the blood is impaired and as a result, intravascular clotting occurs Because of the relatively slow circulation in the venous tree this system is especially vulnerable to such a change For this reason the present discussion will deal primarily with the subject of abnormal blood clotting as it relates to the venous circulation * particularly in the lower extremities

There are several physiologic or pathologic states which are favorable to the initiation of venous thrombosis Among the most important of these are venous stasis direct trauma to the vessel wall and an increase in coagulability of the blood following injury to tissues elsewhere in the body or consequent to changes in the formed elements in the blood stream Of lesser significance are such conditions as factors associated with old age and infectious diseases

* The conditions or agents responsible for arterial thrombosis are presented in the following sections *Pathology* of thromboangiitis obliterans and *Etiology* and *Pathology* of arteriosclerosis obliterans Chap IX Acute Vascular Spasm and *Traumatic Arterial Thrombosis* Chap XVII

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procedures in the pelvis and the intravenous administration of irritants such as *sclerosing* or hypertonic solutions In some individuals even uncomplicated effort or a strain may be sufficient to initiate the process[9, 13] In the causation of the *effort type of venous thrombosis* several factors are involved among which is a very high pressure in the femoropopliteal veins invariably produced during physical exertion[9] Such a force could possibly have a detrimental effect upon a local weak point in the venous tree

Another mechanism is the marked compression of the great veins of the calf which follows sudden and severe or moderate but repeated muscular contractions in the lower limbs As a consequence of such a response there is a violent pumping of venous blood through the relaxed muscular compartment surrounding Hunter s canal which when added to the already high venous pressure present with physical effo t is capable of exerting a bursting force of considerable magnitude The final etiologic factor in thrombosis associated with effort is the marked distension of the venous system which follows venous angulation in the popliteal space as produced by kneeling squatting or tendinous pressure on the popliteal veins If such a state is associated with sudden contraction of the calf muscles trauma to or even rupture of a vein may occur

Th re are several other situations or conditions which may lead to injury of veins For example intimal damage may follow prolonged pressure of the weight of a leg on the calf muscles as frequently occurs during an operation and in the immediate postoperative period when the patient is content to lie on his back without moving The resulting collapse of the veins permits the intimal folds of the vessels to remain in contact with each other thus ultimately leading to irritation and a situation conducive to clot formation A contributing factor is the associated ischemia of tissue due to the pressure Sitting in one position on long trips in busses or trains may also cause trauma to the veins in the lower extremities because of protracted pressure of the seat against these structures A sim lar type of response was noted in England during World War II when elderly individuals we e forced to sleep in reclining chairs in air raid shelters

Malignant invasion of veins can also be considered in the category of local injury The tumor cells may penetrate the wall of the vessel enter the lumen and even proliferate intravascularly Various types of neoplasms may act in this fashion in some instances extending along venous channels for great distances Thrombosis of the vein generally occurs when the adventitia is involved although in some instances it may be delayed until the tumor has reached the lumen of the vessel

Increased Coagulability of the Blood

A variety of different conditions may increase coagulability of the blood Among these is de truction of tissue anywhere in the body as in the case of a surgical procedure accidental trauma extensive burns a delivery or infection Consequent to these states definite changes occur both in the plasma and in the formed elements The alterations in the plasma consist of a greater viscosity and an elevation of the fibrinogen content It has also been suggested that there is a

Venous Stasis

Normal Mechanism of Venous Return Before presenting the various mec anisms which contribute to venous stasis it is necessary to review briefly tl factors normally responsible for the return of blood from the lower extremiti to the heart The most important one is the pumping action of the muscles the legs exerted on the thin walled veins In this manner blood is forced fro distal to proximal segments of vessels and prevented from falling backward l the action of the numerous valves present in the veins of the lower extremitie The continuous entrance of blood into the venous system from the arterial tr also contributes to venous drainage since, as a result the blood already in tl veins is displaced and moved in the direction of the heart

Another factor is bound up with the respiratory excursions of the ches diaphragm and abdominal wall During inspiration the negative pressure in tl chest is elevated by the increase in the size of the thorax in all its diameters ar by a depression of the diaphragm Simultaneously the latter movement and tl contraction of the abdominal muscles raise the positive pressure in the abdomei Through such mechanisms the thin walled inferior vena cava is exposed to higher pressure in its abdominal course and to a lower pressure in its thoraci course a situation which facilitates the movement of blood in an upward directio

Causes of Venous Stasis Most of the factors responsible for such a state ai discussed in *Steps to eliminate or reduce venous stasis*, Chapter XIV and henc at this point it is only necessary to enumerate them Of importance in this regar are physical inactivity, immobilization of a limb the assumption of Fowler position tight abdominal dressings the use of pillows placed under the knee peripheral vasoconstriction frequently associated with the immediate postoper tive period and the presence of varicosities In patients suffering from congestiv heart failure, venous stasis may exist as a result of both the decreased periphera arterial circulation and the increased central venous pressure Venous stasis i also a relatively frequent complication of pregnancy since the increased intra abdominal tension and the pressure of the enlarged uterus on the pelvic vein interfere with the normal venous return from the lower extremities Externa pressure on these vessels by tumors has a similar effect

Of interest in the elucidation of the relative importance of venous stasis as ai etiologic factor in venous thrombosis is the recent finding of early clot formatior in valve pockets, a location which is assumed to be most susceptible to stagna tion of blood[23] An explanation for such an observation may be the following Since to a certain extent a vein depends for nutrition of its inner layers upon absorption of nutrients from the blood in its lumen and since stasis leads to a depletion of oxygen to the living endothelial cells conceivably prolonged stagna tion could produce local morphologic changes which predispose to primary thrombus deposition[23]

Local Injury

Trauma to the intima of a vein may result from a number of different agents Among these are crush injuries to the limb fractures, deep wounds operative

where the endothelium has been injured As a consequence platelet thrombi are formed followed by lysis and the production of thrombin and then by enzymatic action the deposition of a reticulum of fibrin As the initial clot undergoes retraction a serum rich in nascent thrombin is expressed which, if the circulation is sluggish remains in the vicinity of the original process and causes further local clotting [6] The platelet thrombi remain as the head of the thrombus the rest of the clot being known as the body and tail in that order The body which grows laterally as well as longitudinally is composed of fibrin and formed elements of the blood Eventually it fills the lumen of the vessel so as to produce occlusion When the latter process is completed there is more or less fixation of the body of the clot to the wall the degree and extent depending upon the amount of local inflammatory reaction initiated by the foreign body In contrast the tail of the thrombus is not attached to the vessel since it grows longitudinally in the stream of blood before it enlarges laterally Because it is friable it can readily be broken off thus becoming the source of embolic phenomena

A question which has not been fully answered concerns the type of change in the vessel wall consequent to injury which leads to the adherence of platelets to the endothelium Experimental studies have revealed that the formed elements are most likely to adhere to the intercellular cement line a point of lowest surface tension [7,8] After injury to the vessel wall the stickiness of the cement substance appears to increase It has been suggested that trauma allows this material to pass through the endothelial cell to the surface or possibly that the cell by virtue of its fibroblastic potentialities becomes adhesive [7]

Once a thrombus forms several mechanisms come into play to limit its size One is the physical action of the blood in diluting and washing away locally produced thrombotic factors [9] Another is the adsorption of thrombin to the enormous surface of newly formed fibrin reticulum in the clot [9] Other factors involved in checking the spread of thrombosis are plasma antithrombin tissue and blood antithromboplastins and possibly heparin and its plasma co factor circulating fibrinolysin [10] The latter may play a part in dissolving the clot once it has formed Of great importance also is the fact that normal endothelial lining does not encourage clotting

USE OF ANTICOAGULANTS TO COMBAT INTRAVASCULAR THROMBOSIS

In view of the great interest that has developed in the use of anticoagulant therapy in peripheral vascular disorders it has been deemed necessary to devote the present section to this subject Such medication has been employed either as a preventative measure in patients susceptible to thromboembolic diseases or as active treatment of existing arterial or venous thrombosis In the latter situation the primary purpose of the medication is to control or minimize the propagation of the friable tail of an existing thrombus, so as to eliminate the danger of embolism and at the same time allowing the clot to be fixed to the vessel wall by virtue of its foreign body reaction If such a state can be accomplished eventual organization and even recanalization will take place In the

greater tendency toward agglutination of the cellular elements particularly the platelets

Increased coagulability of the blood frequently accompanies visceral carcinoma Although the reported primary sites of the tumor include the stomach lung and gallbladder, the relationship with involvement of the pancreas, particularly of the body and tail of this organ is most striking* While development of venous thrombosis in the area of the tumor is readily understandable (see above), it is much more difficult to explain the appearance of such a process in an extremity when the malignant neoplasm is located in the abdomen The etiology must therefore, be sought in an alteration of the mechanisms associated with coagulation It has been suggested that destruction of tissue by the infiltration of cancerous material liberates substances which, on being absorbed increase the clotting tendency of the blood, similar to that which exists after injury by other means

Certain hematologic conditions are associated with changes which favor blood coagulation Among these is polycythemia in which the responsible factor is probably the greater viscosity of the blood resulting from the increased number of red blood cells The associated rise in platelets and other formed elements may play a secondary role in this regard In the increased tendency to blood clotting observed in severe anemia the explanation in part, may be that in this condition there is a greater than normal clot retraction, resulting in the expression of large quantities of serum containing a high concentration of thrombin Such a situation is conducive to the rapid growth of clots [6]

Other Factors Favoring Venous Thrombosis

There are a number of other unrelated conditions which contribute to venous thrombosis Among these are the changes associated with aging In this regard it is generally accepted that patients in the fourth to the sixth decades are much more susceptible to intravascular clotting than individuals in the younger age groups perhaps because the various *degenerative and neoplastic diseases* are much more common in the former Another possibility is that elderly people are frequently subjected to prostatectomy herniorrhaphy, and gynecologic operations procedures which are associated with venous thrombosis The exaggerated post operative immobility which is a common finding in this age group also plays a role

Various infectious diseases likewise predispose to venous thrombosis In typhoid fever, this state is usually a late complication generally occurring after the fourth week or later in convalescence The left femoral vein is more often involved than any other Influenza rheumatic fever and pneumonia may also be complicated by venous thrombosis

Pathogenesis of Intravascular Clotting

Regardless of the cause it is generally agreed that intravascular thrombosis begins with adhesion of thrombocytes to the intima of a blood vessel at a point

* It is of interest however that carcinoma of the prostate may be associated with a decreased tendency to coagulation

the last dose in the evening should be much larger than the others[4] However, it would seem that a more uniform effect could be expected if the same program were continued throughout the twenty four hour period Regardless of the approach used clotting time determinations are unnecessary since the effect of the heparin is not cumulative and the action of one dose is almost completely dissipated by the time the next one is given

Instead of repeated venipunctures for the intravenous administration of the drug a glass cannula can be substituted[5] This consists of a simple glass observa

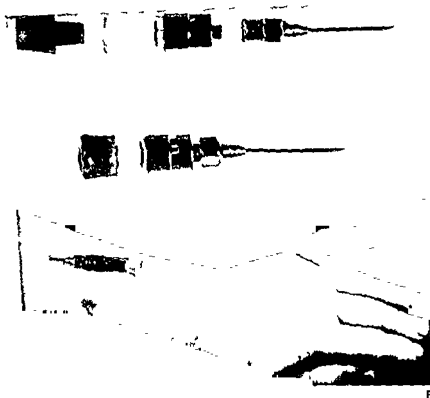


Fig 81 Cannula used for intermittent venous administration of heparin A Different portions of cannula rubber cap glass observation tube and needle unassembled and assembled B Cannula filled with heparin attached to needle in vein (From M C Gephardt G Lavers and D I Abramson Simplified apparatus for multiple blood sampling and venous infusion To be published)

tion tube cut down to approximately ~ 5 cm (1 inch) in length with a Luer Lok connection at one end and a rubber vial cap (hooded type) inserted over the other end (Fig 81) After sterilization by boiling the capped observation tube is filled with heparin solution through the cap using a hypodermic needle attached to a syringe A #~-18 needle is inserted into the selected vein on the dorsum of the hand or forearm and the capped tube filled with heparin is attached to the

presence of pulmonary embolism, anticoagulants are used primarily to prevent further embolic episodes and possibly to minimize propagation of the thrombotic process in the pulmonary bed

Despite extensive application of the therapeutic measure to the point that it has become almost a routine hospital procedure the fact still remains that anticoagulants should never be administered unless dependable laboratory facilities are at hand so that the dosage can be carefully controlled by frequent testing Means should also be readily available for the effective counteraction of any tendency to hemorrhage that might occur in the course of treatment The choice of the proper drug will depend upon the particular case and set of circumstances, and frequently more than one will be used conjointly, at least during the initial stage of therapy

Heparin

Heparin interferes with blood clotting because it is both an antithrombin and an antithromboplastin Its action is immediate although transitory The aim of the therapeutic program is to maintain the venous coagulation time of the blood between 30 and 60 minutes Under these circumstances spontaneous intravascular clotting will be prevented although the already formed thrombus will not be affected except for inhibition of further growth The dosage schedule necessary to produce the desired effect varies considerably from one individual to the other, which makes it impossible to present a standard dose or rate of administration consistently applicable

A number of preparations of heparin are available commercially The material is extracted from animal tissues such as liver, lung and blood and is marketed as the sodium salt dissolved in sterile isotonic solution, with 1 cc containing either 10 50, or 100 mg of heparin

Methods of Administration

Continuous Intravenous Drip This procedure involves the use of an infusion apparatus filled with either 5% glucose in water or isotonic saline solution After the flow is regulated so that approximately 20 to 25 drops are entering the vein each minute heparin is added to the extent of 200 mg of the sodium salt for each 1000 cc of solution, care being taken to dissolve the drug completely Blood coagulation times are performed at least every 12 hours and if less than 30 minutes, then either 25 mg of heparin for each 500 cc of solution remaining is added to the infusion system or the intravenous drip is speeded up Either step is repeated until the clotting time has risen to between 30 and 60 minutes To maintain this level, usually about 10 mg of heparin is required per hour of injection

Intermittent Intravenous Administration Another method consists of the use of single intravenous injections repeated at frequent intervals the most popular schedule being 50 mg every 4 hours during the entire 24 hour period In another plan, 35–50 mg is given every 3 hours Some workers believe that the routine administration of the drug should be discontinued during the night and instead

to such a procedure the necessity for repeated clotting time determinations and the inconvenience and discomfort to the patient inherent in any type of prolonged intravenous injection The intermittent intravenous administration of heparin which has the widest clinical application has in its favor the fact that long periods of immobility in bed and coagulation time readings are not required The disadvantage of repeated venipunctures can be obviated by the substitution of a cannula which at the same time permits the nurse on the floor to give the necessary dosages of heparin thus removing the burden from the house staff The view that there is a disadvantage to the irregular picket fence type of reaction that occurs in the blood stream with intermittent injections of heparin has not as yet been supported by conclusive evidence

There is little question regarding the convenience of giving aqueous or depository heparin subcutaneously or intramuscularly especially if the patient can not be hospitalized Despite this fact the method has not had wide acceptance or application mainly because severe persistent pain may be experienced at the site of injection In an individual already acutely ill such a response must be seriously considered in the evaluation of the method Several attempts have been made to minimize the symptoms among them being the addition of procaine the use of hyaluronidase for rapid dispersion in the tissues an attempt to increase the pH of the depository heparin from 4 to a more alkaline level and the injection of the drug into deep subcutaneous or superficial intramuscular tissues of the anterior or lateral aspect of the thigh * so that the site will not be subjected to the weight of the body However none of these steps has been particularly successful

Another disadvantage to the use of heparin in retarding media is that the material will be partly fixed to the tissues and partly neutralized by thromboplastic substances in the tissue fluids thus permitting only a fraction of the original dose to reach the blood stream [18] This may create the danger that the minimum effective concentration in the blood will not be reached At the same time because of prolonged absorption it may be difficult to control bleeding once it appears

Prevention and Treatment of Bleeding from Heparin

When heparin is given in the immediate postoperative period there is always the possibility of some bleeding from the surgical wound Careful attention should therefore be paid to hemostasis if the use of this medication is contemplated Ordinarily approximately 4 hours are allowed to elapse before beginning the therapy in order to determine whether or not spontaneous bleeding is going to take place In every case the wound must be carefully watched during the entire period of administration for slight oozing may be increased to a marked extent if the medication is continued On the other hand withdrawal of heparin usually controls any bleeding tendency since the action is so transient

Should bleeding persist as may occur in the use of continuous intravenous

* In deep thrombophlebitis the involved thigh should not be used as a site of injection until the swelling has partially receded

needle The apparatus is securely taped in place and then the desired quantity of heparin is injected into the system, this in turn displacing an equal amount which enters the blood stream Subsequent doses are administered at the appropriate times in the same manner If care is taken in the insertion of the needle and if this is done in a site which is not exposed to much movement the apparatus can generally be used for 2 days without clotting occurring in the needle

When further heparinization is necessary, it is advisable to use another vein, since otherwise the continuous irritation of the needle against the intima of the vessel will eventually produce thrombosis despite the counteracting effect of the heparin

Subcutaneous or Intramuscular Route The administration of heparin by this means has had a clinical trial in recent years[34 36] the drug is given either in a vehicle such as Pitkin menstruum or gelatin or as an *aqueous solution with or without* hyaluronidase In the depository form heparin exerts an effect three or four times as long as that produced by the aqueous solution

The schedule for heparin in Pitkin menstruum* or in a gelatin vehicle alone (Depo Heparin Sodium) *is similar The initial dosage for patients weighing up* to 70 kg (approximately 150 lb) is 300 mg while for heavier individuals 400 mg should be given If the coagulation time is increased by the first dose from a control level of 9–15 minutes to 30–60 minutes, an adequate heparin effect has been obtained *and subsequently* 300 mg *administered every second day throughout* the period of heparinization should be enough to maintain this level However it is still necessary to check the coagulation time at intervals of 12–14 hours for the first 48–72 hours and daily or every second day during the remainder of the period of treatment *The determination each time should immediately* precede the injection of the drug Since Depo Heparin is solid at room temperature it is necessary to liquefy it by warming the container in hot tap water before attempting to inject the material

In the intramuscular or subcutaneous administration of an aqueous solution of heparin, best results are obtained if such a procedure is preceded by an intravenous *dose of 100 mg in order to facilitate prompt action* Then the effect *is* maintained through the use of subcutaneous or intramuscular injections of 50–75 mg *of the concentrated material (50 mg/1 cc) every 4–6 hours The addition of* hyaluronidase (500 viscosity units) in the same syringe may be of value in reducing the associated pain *(see below)*

Evaluation of the Various Methods of Administration

The best method of administration can be chosen only after consideration of the relative merits of each for the particular case For example the continuous intravenous *infusion of the drug is indicated if in the* face of potential bleeding it is necessary to obtain a consistent and sustained yet moderate prolongation of the clotting time[11] However there are several objections

* This consists of heparin combined with 18% gelatin 8% dextrose 0 5% glacial acetic acid and sufficient distilled water to make 100% The material is available in the form of 2 or 3 cc ampules each cubic centimeter containing 200 mg of the sodium salt of heparin

to such a procedure the necessity for repeated clotting time determinations and the inconvenience and discomfort to the patient inherent in any type of prolonged intravenous injection The intermittent intravenous administration of heparin which has the widest clinical application has in its favor the fact that long periods of immobility in bed and coagulation time readings are not required The disadvantage of repeated venipunctures can be obviated by the substitution of a cannula which at the same time permits the nurse on the floor to give the necessary dosages of heparin thus removing the burden from the house staff The view that there is a disadvantage to the irregular picket fence type of reaction that occurs in the blood stream with intermittent injections of heparin has not as yet been supported by conclusive evidence

There is little question regarding the convenience of giving aqueous or depository heparin subcutaneously or intramuscularly especially if the patient cannot be hospitalized Despite this fact the method has not had wide acceptance or application mainly because severe persistent pain may be experienced at the site of injection In an individual already acutely ill such a response must be seriously considered in the evaluation of the method Several attempts have been made to minimize the symptoms among them being the addition of procaine the use of hyaluronidase for rapid dispersion in the tissues an attempt to increase the *pH* of the depository heparin from 4 to 7 more alkaline level and the injection of the drug into deep subcutaneous or superficial intramuscular tissues of the anterior or lateral aspect of the thigh * so that the site will not be subjected to the weight of the body However none of these steps has been particularly successful

Another disadvantage to the use of heparin in retarding media is that the material will be partly fixed to the tissues and partly neutralized by thromboplastic substances in the tissue fluids thus permitting only a fraction of the original dose to reach the blood stream[16] This may create the danger that the minimum effective concentration in the blood will not be reached At the same time because of prolonged absorption it may be difficult to control bleeding once it appears

Prevention and Treatment of Bleeding from Heparin

When heparin is given in the immediate postoperative period there is always the possibility of some bleeding from the surgical wound Careful attention should therefore be paid to hemostasis if the use of this medication is contemplated Ordinarily approximately 4 hours are allowed to elapse before beginning the therapy in order to determine whether or not spontaneous bleeding is going to take place In every case the wound must be carefully watched during the entire period of administration for slight oozing may be increased to a marked extent if the medication is continued On the other hand withdrawal of heparin usually controls any bleeding tendency since the action is so transient

Should bleeding persist as may occur n the use of continuous intravenous

* In deep thrombophlebitis the involved thigh should not be used as a site of injection until the swelling has partially receded

administration or with depository heparin protamine sulfate is indicated t neutralize the coagulation defect The desired effect occurs immediately afte intravenous administration the amount necessary is 50–75 per cent of the quan tity of heparin previously given Transitory flushing and warmth may follow th use of protamine while extravasation may produce considerable irritation locally [1] It is also necessary to point out that an excess of this drug may actually increas coagulability Blood transfusions have likewise been utilized to combat bleeding but rarely is such a procedure necessary, since the other much simpler measure are generally sufficient to control the situation

Bleeding during the administration of depository heparin can be controlled in a number of ways An ice pack applied to the site will sharply reduce the rate o absorption as will a tourniquet placed proximally if this is possible At time an intramuscular injection of protamine locally may be required, in order to neutralize the heparin still present

Contraindications to, and Caution in, Use of Heparin

In the presence of certain conditions heparin should not be used at all, while in the case of others, it may be given if the therapeutic indication outweighs the associated risk It is contraindicated in all clinical entities in which there is a tendency to bleeding such as hemophilia purpura hemorrhagica obstructive *jaundice or severe liver disease There is also a possibility that it will cause* hemorrhage from cerebral vessels in patients with subacute bacterial endo carditis For the same reason it should not be given after recent intracranial or intraspinal surgery The drug should be used with caution following pros tatectomy or in the presence of ulcerative lesions of the gastrointestinal tract drainage tubes in operative wounds and tubes in the renal pelvis or the common bile duct However there is no evidence to indicate that heparin has a deleterious effect on wound healing [17]

Dicumarol (Bishydroxycoumarin)

In recent years dicumarol has almost superseded heparin as the drug of choice in the prevention and prolonged treatment of acute deep venous thrombosis and pulmonary embolism First isolated in spoiled sweet clover [18] it was considered to be the responsible agent for the hemorrhagic disease which affects cattle Sub sequently, a product was synthesized which was found to be identical in bio logic characteristics with the active principle in spoiled sweet clover and it is this substance which is available commercially as dicumarol [18]

The exact mode of action of dicumarol is not known However, there is some evidence to indicate that it suppresses the synthesis of prothrombin in the liver and thus inhibits clotting since prothrombin is a necessary initial constituent in the ultimate formation of fibrin The drug appears to have its effect by inhibiting utilization of vitamin *K rather than by a direct action on prothrombin* When administered to human beings it produces a prolongation of the prothrombin time and in large doses has a similar effect on the venous clotting time It will prevent intravascular clotting and the growth of an already existing thrombus but it will not in any way dissolve a clot which is already formed

Method of Administration

The use of dicumarol is associated with a certain amount of risk particularly through excessive bleeding Except in very special circumstances a patient on this medication should be under observation in a hospital and the house staff should be well versed in the administration of the drug as well as in the methods for combatting any untoward responses The patient should be interviewed before

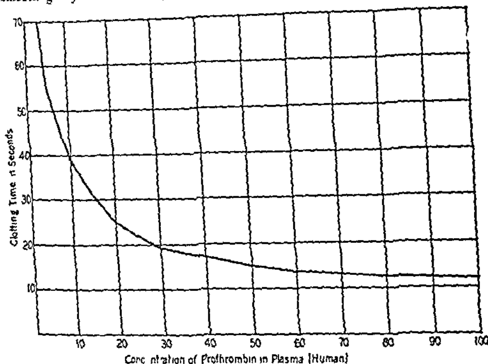


Fig 8 Graph demonstrating the relationship of the coagulation time of recalcified plasma (with excess of thromboplastin) to the concentration of plasma used in the quantitative determination of prothrombin in human plasma (Reproduced through the courtesy of A J Quick The clinical application of the hippuric acid and the prothrombin tests *Am J Clin Path* 10 - 1940)

therapy is started in order to determine whether or not any of the contraindications listed below exist and he should be carefully observed during the entire period of treatment

The aim of the therapeutic program is to maintain the prothrombin content of the blood at approximately -o per cent of normal using the Quick curve (Fig 8-) * No set rule can be followed in the administration of the medication and the only guide is the height of the daily prothrombin time and the rate of

sma in the presence of an the amount of thrombin blood Two processes con ... to the length of the prothrombin me the period necessary for th conversion of prothrombin to thrombin and the time taken for thrombin enzymatically to convert fibrinogen to fibrin

fall of the level on previous days It is generally advisable to perform a prothrombin time determination preliminary to the administration of dicumarol, since in this manner, previously unrecognized liver pathology may be uncovered If the control reading is already low, the drug should be given cautiously or not at all The individual with a normal percentage of prothrombin time (approximately 80–100 per cent) can readily tolerate an initial dose of 300 mg followed by 200 mg on the second day and 100 mg on the third Nevertheless it is important to do daily prothrombin time determinations during this period since a rapidly falling level may indicate a marked responsiveness to the medication and necessitate cautious control of subsequent dosage In most instances, however, a significant reduction in the percentage of prothrombin time does not occur before the third day of administration, when the patient has had a total of 600 mg of the drug It is important to point out that unless such a reduction takes place shortly after therapy is started, intravascular clotting may not be prevented On the other hand a drop much below 20 per cent may result in severe and dangerous bleeding from various portions of the body

Following the period of high dosage, the quantity of dicumarol necessary to maintain the desired level of prothrombin time varies considerably from patient to patient and even from day to day in the same individual Some may require as little as 25 mg daily while in others 100 mg or more may be necessary To determine the proper amount daily prothrombin time determinations should be carried out during the entire period of administration of the drug It is imperative that the results of this procedure be consistently reliable for otherwise serious bleeding may follow On occasion when the readings obtained over a week end are out of line with those anticipated on the basis of the quantity of drug administered explanation may be found in the fact that a substitute technician is performing the tests Under such circumstances it is perhaps wiser to disregard the laboratory results and decide upon the size of the dose from the responses obtained on previous days

Since the patient on dicumarol may be taking other medications it is necessary to mention those common therapeutic procedures which as a side reaction are considered as having an effect on the clotting mechanism It has been suggested that both penicillin and digitalis preparations increase the coagulability of the blood, but the evidence on this point is by no means clear-cut However, it appears much more certain that large doses of aspirin and other salicylates can induce hypoprothrombinemia and hemorrhage The action of salicylates and dicumarol are regarded as essentially the same except that the former are much less powerful

Prevention and Treatment of Bleeding from Dicumarol

Precautions It is necessary to warn the patient under effective dicumarol therapy *against traumatizing the mucous membrane* of his nose cutting his face while shaving, or having teeth removed since severe bleeding may ensue under these circumstances In fact at times death may occur from hemorrhage despite attempts to counteract the hypoprothrombinemia

Value of Prothrombin Time Determinations Although a greater than thera

peutic depression of prothrombin level by dicumarol may be followed by bleeding there is not necessarily a direct relationship between the degree of prothrombin activity and the presence or absence of hemorrhagic tendency In other words in some patients the percentage of prothrombin time may be markedly decreased and still no signs of bleeding will occur while in others hemorrhage may be present despite the fact that the therapeutic range is only moderately exceeded It is obvious therefore that the level of prothrombin in the blood is only one of several factors that determine whether or not a bleeding tendency will become apparent

Usual Sites of Involvement Several portions of the body have a predilection for hemorrhagic manifestations Among these are the skin particularly of the legs and dorsum of the feet the kidneys * the perirenal fatty tissue and the brain Hemorrhage around the kidney produces pain in that area and the formation of a palpable tender mass while in the brain it may cause the appearance of various psychic changes depending upon the site of involvement Although it is understandable why traumatizing the mucous membrane or skin might produce extensive hemorrhage if the patient is under the therapeutic effect of dicumarol it is much more difficult to explain the apparently spontaneous change of this type in the kidney substance Evidently dicumarol causes certain changes in the permeability of the capillaries as well as a depression of prothrombin activity

Measures to Control Hemorrhage In case bleeding occurs either from the operative site or from other parts of the body *the first step is to discontinue the drug* In the presence of hematuria alone subsequent specimens of urine should be watched carefully If the amount of blood becomes less or disappears it is advisable to do nothing until the percentage of prothrombin time has reverted to the therapeutic range as a result of the normal production of prothrombin by the liver When this has been accomplished and if the need for anticoagulants still exists dicumarol should be started again and given even more cautiously

In the presence of obvious bleeding or persistently falling prothrombin activity despite discontinuation of dicumarol other steps should be carried out Until recently menadione bisulfite (water soluble synthetic vitamin K) has been used for this purpose the drug generally being given intravenously in the equivalent of 60 mg doses not more often than once daily However a number of reports have appeared in the literature to indicate that this type of preparation has a variable and usually delayed effect in reversing dicumarol induced hypoprothrombinemia [10, 31] It appears to be most effective when the last dose of the anticoagulant has been small and none has been given for 24 hours or longer Because of these weaknesses the water soluble preparations have been for the most part superseded by the use of the oil soluble forms of vitamin K (vitamin K_1 and K_1 oxide) [14, 20, 29] Fifty milligrams of the latter when given intravenously in the form of an emulsion will frequently reverse the hypoprothrombinemia induced by dicumarol to normal or nearly normal levels in approximately 6 hours regardless of the degree of depression or the amount of recently administered anticoagulant [3] If excessive quantities of dicumarol have been given the 50 mg dose may have to be repeated several times at 6–12 hour intervals However it is

Becau one of the ... to have repeated ... it is advisable

necessary to point out that too heroic treatment with vitamin K_1 may defeat the purpose for the original use of anticoagulants i e, to prolong the prothrombin time, *and actually induce thrombosis Ideally the medication should be given* in sufficient amount to lower the prothrombin time to halfway between the therapeutic level and normal, admittedly a difficult feat to accomplish

Another procedure which has been used to counteract bleeding following excess dicumarol administration is transfusion of fresh citrated blood or of lyophilized plasma Since it has recently been found that storage does not alter the component of prothrombin necessary for coagulation,[74] it may be that blood from a blood bank can be substituted for fresh citrated blood if the latter is not readily available However, in either case it must be realized that the actual amount of prothrombin and related factors in a transfusion of 500 cc of blood is so small compared with the existing circulating blood volume that aside from replacing lost blood such a measure may have little effect on the clotting mechanism

Contraindications to, and Caution in, Use of Dicumarol

There are absolute and relative contraindications to the administration of dicumarol, similar for the most part to those already enumerated in the case of heparin Since the drug is excreted by the kidneys it is also necessary to add renal insufficiency to the list for in this condition the concentration of dicumarol may rise rapidly and thus cause hemorrhage In patients with right heart failure and systemic and hepatic congestion the reaction to the usual dosages of the medication may be intensified sometimes to the extent that a dangerous degree of hypoprothrombinemia *is induced* Extra care *is* required under these circum stances

Therapeutic Applicability of Heparin and Dicumarol*

Individual Advantages Heparin possesses certain distinctive therapeutic char acteristics It is invariably effective quick acting easily controlled and readily neutralized Furthermore *it inhibits platelet agglutination even before there is* any obvious change in coagulation time[3]

The main advantage of dicumarol is that once a therapeutic level of depression *of prothrombin activity has been achieved it can generally be maintained* without too much difficulty Another consideration is the fact that it is relatively inex pensive to administer a point of importance if a protracted period of anti coagulant therapy *is* contemplated

Therapeutic Application Considerable clinical evidence exists to support the view that both heparin and dicumarol are potent therapeutic agents in intravas cular clotting *The prompt administration of heparin in the early stage of deep* thrombophlebitis causes a reduction in the duration of the stay in bed in the mortality rate and in the severity and incidence of the postphlebitic syndrome[1, 19] Such effects are probably *due to the action of the drug in preventing the propa* gation of the thrombus into other channels For the same reason heparin is of

* See Table 18

great value in the early stage of arterial occlusion Dicumarol has a similar therapeutic effect in these disorders except that its action is delayed When used in conjunction with vein ligation this medication appears to reduce the possibility of a thrombus forming proximally to the level of the ligature thus decreasing the incidence of pulmonary emboli from such a source

Individual Disadvantages There are several objections to the administration of heparin First is the expense associated with the use of the medication for any prolonged period of time Second unless intermittent injections are utilized frequent clotting time determinations are required in order to maintain a therapeutic level in the blood Third except when combined with a retarding medium the effect of the drug disappears within 4 or 5 hours after its discontinuation As a result of this transient and nonaccumulative action of heparin intravascular clotting and pulmonary embolism can still occur shortly after therapy has been terminated In fact, sudden withdrawal tends to cause *increased coagulability* of the blood *

There are also several practical disadvantages to the use of dicumarol the most important being the delay of 36 to 72 hours before there is a clinically valuable reduction in the percentage of prothrombin time Therefore when an immediate anticoagulant action is required as in the treatment of the acute stage of arterial occlusion deep thrombophlebitis or pulmonary embolism this drug by itself is of little use A characteristic of dicumarol which may on occasion cause serious consequences is the prolongation of the depression of prothrombin activity for *several days after* termination of the medication for this property makes bleeding more difficult to control Finally a disadvantage which is common to most anticoagulants is the fact that repeated prothrombin time determinations are essential in order to regulate the dosage of the drug

Combined Administration of Heparin and Dicumarol

By the use of heparin in conjunction with dicumarol the undesirable actions of each are for the most part counteracted while their therapeutic effects are enhanced Such a program is essential in the early stage of acute arterial thrombosis and embolism acute deep thrombophlebitis and pulmonary embolism for reasons already given The procedure is as follows

A prothrombin time determination is performed and dicumarol therapy is initiated according to the program described above At the same time 50 mg of heparin is given intravenously through a cannula and repeated at 4 hour intervals for at least the next *48–72 hours* By then prothrombin activity should have fallen sufficiently as a result of the dicumarol therapy to make it safe to discontinue the heparin medication Thereafter the function of maintaining a reduced clotting tendency of the blood is carried on by the use of dicumarol alone in the manner already indicated In the event that the prothrombin level is not depressed by dicumarol to the desired extent by the second day then heparin is continued until this is accomplished

* For this reason it is necessary to continue the administration of the drug for a number of days after the patient becomes ambulatory and then taper off the dosage by increasing the intervals between medication

Table 18 Comparison between Heparin and Dicumarol

	Heparin	*Dicumarol*
Source of drug	Prepared from animal liver or lung tissue	Synthesized originally extracted from spoiled sweet clover hay
Mode of action	Prevents liberation of thromboplastin from platelets with aid of plasma co-factor, it prevents *conversion of prothrombin to* thrombin forms with serum albumin a strong antithrombin	Inhibits formation of prothrombin in liver impairs clot retraction in large *quantities prolongs clotting time*
Onset of action	Almost immediate	Delay of 36-72 hours after beginning of administration
Duration of action	In aqueous solution action is transient disappears in several *hours no cumulative effect in* gelatin or Pitkin menstruum action is prolonged 24 hours or more	Prolonged effect may still be present 2-10 days after *administration is stopped*
Contraindications	Blood dyscrasias with bleeding tendencies hemophilia thrombocytopenic purpura before surgery in conditions in which even a small amount of bleeding might cause serious consequences as after recent operation on brain and spinal cord in subacute bacterial *endocarditis*	Same as in case of heparin
Conditions in which drugs should be used with caution	Ulcerative lesions in gastrointestinal tract open wounds tubes in renal pelvis or *common* bile duct or tubes in mouth or nose	Liver disease or in malnutrition ulcerative lesions in gastrointestinal tract open wounds tubes in renal pelvis or common bile duct
Therapeutic *applications*	Myocardial infarction prevention *of venous thrombosis in susceptible* individuals treatment of deep venous thrombosis and pulmonary embolism treatment of arterial embolism and postembolectomy stage repair of traumatized arteries acute stage of frostbite	Generally the same as for heparin *in order to* continue therapeutic effect of little use if immediate effect is necessary as in acute phase of occlusion of arterial or venous channels pulmonary embolism or frostbite
Methods of administration	Continuous intravenous *drip* intermittent multiple intravenous injections intermittent *multiple* spaced intramuscular injections subcutaneous injection in retarding media (gelatin vehicle or Pitkin menstruum)	*Oral route*
Plan of administration	Aqueous heparin 50 mg intravenously *every 4 hours heparin in* gelatin 200-400 mg subcutaneously every 48 hours heparin in Pitkin menstruum 400 mg. subcutaneously for first dose followed *by 300 mg every 48 hours* repeated blood coagulation times necessary for last 2 procedures but not for first	*300 mg the first day followed by 200 mg* the second and 100 mg the third day plan modified as result of effect on daily prothrombin determinations

Table 18 (continued)

	Heparin	*Dicumarol*
Form and concentrations clinically available	Aqueous heparin sodium in 3 concentrations 10 mg 50 mg and 100 mg per cc heparin sodium in gelatin 200 mg in 1 cc heparin sodium in Pitkin menstruum 100 mg in 1 cc	100 50 and 25 mg tablets
Tests for control of dosage	Blood coagulation time determination (modified Lee White (Howell) method)	Prothrombin time determination (one- or two stage test)
Laboratory indication of desired therapeutic effect	A three or four fold increase in blood coagulation time (a rise to 30 to 45 or 60 minutes from a control level of 9 to 15 minutes)	A fall in prothrombin activity to 20% of normal (Quick curve)
Untoward effects	Bleeding from gums and mucous membrane of nose and conjunctiva purpura hematuria bleeding into perirenal fat	Same as in case of heparin
Means to combat bleeding tendency	Discontinuation of drug use of protamine sulfate occasionally transfusion of whole blood in case of subcutaneous route use of ice bag over area and tourniquet proximally to it if possible	Discontinuation of drug use of natural vitamin K_1 or transfusion of whole fresh blood
Cost of therapy	Relatively quite expensive	Relatively inexpensive

Care must be taken that during joint administration of heparin and dicumarol blood for the prothrombin time determination is not drawn while heparin is still active in the blood stream It has been shown that any quantity of heparin in the sample will definitely decrease the percentage of prothrombin time and thus mislead the physician in his administration of dicumarol If single intravenous doses of heparin are being given the best time to obtain a blood sample is just before the next injection at a time when the pharmacologic effect is at a minimum With the use of a continuous drip dependable prothrombin levels can not be obtained When depository heparin is administered the amount that is present in a blood sample at any one time is evidently not of sufficient quantity to alter prothrombin activity significantly

NEW ANTICOAGULANTS

Several new anticoagulants have recently appeared in the literature but these have not received sufficient clinical trial for complete evaluation The one most extensively investigated is Tromexan also called B O E A Others include BL5 Compound No 63 phenylindandione and Paritol All of these but the last are coumarin derivatives chemically related to dicumarol and their pharmacologic action is also the same Paritol has an effect on clotting time similar to that of heparin

Tromexan [bis 3 3 (4 Oxycoumarinyl) Ethyl Acetate] This substance possesses certain advantages and disadvantages as compared with dicumarol. It has an earlier onset of action, so that a therapeutic prothrombin level is generally attained in 18–24 hours as compared with a lag period of 36–72 hours for dicumarol. Furthermore, it is more rapidly detoxified, and as a result, the danger incidental to cumulation is minimized. Because of its relatively rapid reversibility of action the untoward effects associated with an excess dosage of the drug are more readily controlled. However, it is much more expensive to maintain a patient on this medication than it is with dicumarol. Another disadvantage is the marked daily fluctuation in percentage of prothrombin activity that occurs with Tromexan.

Tromexan is administered orally, the drug being obtained in the form of tablets of 150 and 300 mg. With an initial dose of 1200–1800 mg most individuals will manifest a therapeutic prothrombin level within 24 hours, although it generally takes about a week before the patient is well stabilized on the medication. In order to maintain a more constant therapeutic effect on prothrombin activity it is advisable to use divided doses of the medication on an 8 hour schedule. The total quantity administered daily varies between 300 and 900 mg. As in the case of dicumarol, the most effective antidotes for excessive hypoprothrombinemia induced by Tromexan are vitamin K_1 and K_1 oxide.

Phenylindandione (PID Hedulin) This drug has been described as an anticoagulant intermediate in action between heparin and dicumarol.[6] An initial dosage of 200 mg, in two divided amounts morning and evening, is generally sufficient to depress prothrombin activity to a therapeutic level. On the second day 100 mg is administered, the average daily quantity necessary thereafter being approximately 65 mg. In some instances however patients may be found to be relatively refractory to PID and under such circumstances may require initial amounts as high as 1000 mg and a daily maintenance dose of as much as 300 mg. After the drug is stopped it takes an average of 48 hours for the percentage of prothrombin time to return to its original level.

No major toxic effects of PID have been reported other than the hemorrhagic complications common to agents producing hypoprothrombinemia. There may be some initial albuminuria which usually disappears after several days of therapy.[8] The urine may become orange red in color, but this has been shown to be related solely to color development by PID in an alkaline solution. Again the intravenous injection of natural vitamin K_1 will counteract a marked fall of prothrombin activity produced by an overdosage of PID. It is advisable to use a minimal effective dose (5–50 mg) since this prevents the refractory period seen with large quantities should readministration of PID be desired.

PID has several advantages over the other anticoagulants. It produces a quicker response than dicumarol and there is less danger of toxicity. Although it is not as rapid in action as Tromexan its more protracted effect makes it much easier to maintain a therapeutic prothrombin level over a prolonged period. In fact this uniform response permits a reduction in the necessary number of prothrombin time determinations to two or at the most three times a week.[5] The variation in individual susceptibility to phenylindandione appears to be less than with dicumarol or Tromexan.

Compound No 63 (2 Methyl 2 Methoxy 4 Phenyl 5 Oxodihydropyrano (3 2 c) (1) Benzopyran) This drug also produces a somewhat more consistent hypoprothrombinemia with less tendency to daily fluctuation than does Tromexan[3] However the effect persists for a longer period after administration is discontinued The dosage is 100–150 mg on the first day and 25–50 mg on the second Thereafter the guide to dose and frequency of administration is the effect on the prothrombin level As in the case of Tromexan vitamin K_1 is a strong antagonist for No 63 terminating the hypoprothrombinemia in 24–48 hours

Paritol (Sulfate Mannuronic Acid) This drug is a rapidly acting synthetic anticoagulant which prolongs clotting time for 8–12 hours after an intravenous injection In contrast the effect of heparin with a single intravenous dose is 4–5 hours However the drug may produce occasional toxic effects such as a further rise in blood urea nitrogen in the presence of kidney disease a severe general reaction with vascular collapse and swelling of the hands and feet[33] These undesirable reactions either clear up spontaneously or respond to treatment with epinephrine

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CHAPTER

XXX PHARMACOLOGIC ACTION OF AGENTS THAT PLAY A ROLE IN PERIPHERAL VASCULAR DISORDERS

VASODILATOR DRUGS

In the past decade a large number of drugs have been advocated in the treatment of peripheral vascular disorders because of their vasodilating action. Most of them have had a short-lived, although at times enthusiastic, reception at the hands of the clinician who is always seeking for a means of increasing blood supply to a limb with an impaired circulation.

There are several objections which apply in varying degrees to all vasodilating medications. First, their pharmacologic action generally does not persist so that it is necessary to administer them at frequent intervals if a therapeutic level is to be maintained. Second, many of the drugs have severe side reactions which make their prolonged usage impracticable. Finally, a number of them, particularly some of the sympathetic blocking agents, produce widespread vasodilatation which might cause a fall in systemic blood pressure of sufficient magnitude to produce a decrease in the amount of blood reaching the limb. Under such circumstances, despite the concomitant vasodilatation, the rate of local blood flow might actually be reduced.*

Use in Organic Vascular Disorders. When one considers the type of pathologic changes present in blood vessels affected by a chronic occlusive arterial vascular disease, it is understandable why vasodilating drugs are for the most part ineffective under these circumstances. However, they do exert a therapeutic influence on those compensatory collateral channels not involved in the disease process with the result that there is some *augmentation in* cutaneous circulation to the distal portion of the limb. For this reason vasodilating drugs are of some value in the treatment of an ulcer or gangrene. On the other hand, there is no physiologic evidence to indicate that these measures increase muscle circulation and hence their use in the presence of intermittent *claudication* has no basis. In

* Such a response can usually be counteracted by having the patient lie in the supine position during and for a short time after the administration of the medication.

general therefore, it can be stated that vasodilating drugs have a very limited application as therapy in chronic occlusive arterial vascular diseases

Use in Functional Vascular Disorders Where vasospasm predominates, the administration of vasodilating drugs may be of definite therapeutic value Although the increase in circulation is only transient if the drug is given often enough, it may cause an overlapping and hence a prolonged beneficial effect Furthermore, if a reflex arc is responsible for the vasospasm, repeated removal of its influence may be sufficient to effect a permanent cure eventually Certain occlusive arterial vascular conditions are associated with varying degrees of vasospasm and in these too, elimination of such an effect by the use of vasodilators is a worthwhile procedure

Methods of Administration

In the study of a vasodilating drug it is necessary to determine first whether the available means of administration produces the greatest pharmacologic effect and second whether it is the most practicable Unfortunately in many instances no one avenue combines both these advantages *

Oral Route This method is the simplest since it does not require the attendance of a physician and since it permits repeated administration of the drug during the course of the day thus maintaining a more prolonged vasodilating effect However several of the medications are not available for oral use while others when given in this manner may produce severe gastrointestinal symptoms

Intravenous Route There is little question that by this means a much greater pharmacologic effect of the drug can be expected than by oral administration but the possibility of untoward response is likewise increased Furthermore with such a procedure if vasodilatation does occur it is generally widespread and particularly marked in those vascular beds capable of normal dilatation As a result there may be diversion of blood from the narrowed lumen of diseased vessels into other more normal channels Obviously such a response would have an untoward rather than a beneficial action upon the nutrition of the already poorly nourished digit or digits Despite such theoretical objections however, many of the vasodilating drugs have been given intravenously in extensive clinical trials without the subsequent appearance of nutritional disturbances

Intra arterial Route For the elicitation of the greatest possible degree of vasodilatation in the limb with an impaired circulation this mode of administration is the best If the dose and speed of injection are carefully regulated very little of the medication will reach the general circulation, with the result that systemic and side reactions are minimized At the same time the high concentration of the drug in the affected tissues lengthens the duration of the period of increased circulation

However, there are certain objections or disadvantages to intra arterial administration First, because of the special type of technic and the aseptic precautions

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necessary this approach should only be carried out by those experienced in the procedure preferably in a hospital or clinic Second, *although an occasional* intra-arterial injection of a vasodilator will have no danger associated with it, routine use may lead to untoward reactions For when there is need for such an approach the femoral artery is rarely normal with the result that repeated penetration of this vessel may lead to local trauma spasm and even thrombosis Obviously if the artery is partially or completely occluded the procedure is not applicable Because of such objections, it is generally not practicable as therapy in the chronic stage of an occlusive arterial vascular disorder, although perhaps useful in the presence of an acute trophic disturbance It must also be pointed out that drugs which are ganglionic blocking agents like Etamon and hexamethonium should not be given *in such a manner*, since they have no effect on the neuroeffector organ in the blood vessel wall (see below)

Ion Transfer This is a procedure which has a limited but definite application in peripheral vascular disorders The technic indications and contraindications are presented in *Ion Transfer* Chapter XXV

DRUGS HAVING AN INHIBITORY ACTION ON THE SYMPATHETIC NERVOUS SYSTEM

There are a number of medications which have been utilized as therapy in peripheral vascular disorders because of their blocking effect on the sympathetic nervous system Some act by depressing the vasomotor center, thus reducing the number of vasoconstricting impulses which reach the peripheral blood vessels Others produce a blockade of the paravertebral sympathetic ganglia while still others exert their inhibitory influence on the neuroeffector organ in the blood vessel wall Several have more than one action Regardless of the site of blockade in each instance an augmentation in cutaneous circulation occurs in the extremities as a result of removal of vasomotor tonus and passive dilatation of the vessels

The introduction of these chemical blocking agents represents a definite advance in the medical treatment of peripheral vascular disorders They appear to produce a much more consistent more prolonged and greater increase in blood flow than do other types of vasodilators (see below) Furthermore those which act on the neuroeffector organ in the blood vessel wall are of value when sympathectomy is followed by re-establishment or exaggeration of tonus, a situation with which it is ordinarily difficult to cope However, it must be pointed out that the augmentation in circulation to a limb produced by most of the sympathetic blocking agents is generally not as great as that brought about by local sympathetic denervation through sympathectomy or paravertebral sympathetic block

Drugs Having a Depressant Effect on the Vasomotor Center

There are a number of drugs which tend to reduce the rate of formation of vasoconstrictor impulses in the vasomotor center Among those which act directly are Hydergine[1] oral alcohol inhalation anesthetics and intravenous procaine The production of a fever through the parenteral administration of a nonspecific protein also depresses the vasomotor center but this is accomplished indirectly

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perature of the toes and in blood flow to the foot[40] However, as in the case of Etamon the neuroeffector organ in the blood vessel wall is still responsive to various adrenergic agents

Clinical reports are too few for the proper evaluation of hexamethonium in peripheral vascular disorders It may be useful in the acute stage of deep thrombophlebitis[19] and in causalgia[5] for the relief of pain and in sudden occlusion of main arteries to combat the associated spasm of the collateral vessels It is questionable as to whether the drug has any value in the chronic stage of arteriosclerosis obliterans or thromboangiitis obliterans

There are several disadvantages to the parenteral administration of hexamethonium One is the resulting state of severe postural hypotension particularly after the initial dose In fact there may also be a reduction in supine blood pressure For this reason it is advisable to administer the drug very cautiously in hypertensive or debilitated patients[18] Before giving the full blocking dose it is best to try small quantities intravenously and determine the change in blood pressure If there is a marked fall the injection should be halted immediately It is of interest that with repeated administrations the hypotensive effect becomes less marked

An undesirable reaction to the prolonged use of hexamethonium is the development of constipation On occasion a condition resembling paralytic ileus occurs with distension nausea and abdominal cramps[18] In view of such severe side reactions it is quite possible that hexamethonium will never assume an important role as therapy in peripheral vascular disorders

Adrenergic Blocking* Agents†

Priscoline (2-Benzylimidazoline Hydrochloride) This drug acts at the periphery to combine with the receptor substance in the neuroeffector organ thus inhibiting the response of the latter to vasomotor stimulation and circulating sympathomimetic agents Its pharmacologic effect is limited to the production of vasodilatation and increased blood flow through removal of normal or abnormal vasomotor tonus Plethysmographic studies in man have revealed a consistent increase in circulation to the foot and leg ranging from 30 to 110 per cent over the control readings the augmentation occurring in the skin and subcutaneous tissues with an actual decrease being present in the muscles[31] The drug is also effective in raising the skin temperature of the digits[37]

Priscoline has had extensive clinical trial It appears to be most effective when vasospasm is the predominant pathologic response as in Raynaud s disease[21] or when there is a definite vasospastic element superimposed on an arterial or venous occlusive vascular disorder as in the acute stage of arterial embolism or deep thrombophlebitis It may also be worthwhile in the treatment of ulceration in thromboangiitis obliterans and arteriosclerosis obliterans The drug can be administered orally intramuscularly intravenously and intra arterially[9]

* The terms sympatholytic and adrenolytic have been commonly substituted for adrenergic blocking but there is little basis for such usage

† See Fig 80 p 438

through the intermediary of the temperature regulatory center in the hypothalamus

Several of the above procedures have clinical application Hydergine, oral alcohol, and intravenous procaine are worthwhile adjuncts in the treatment of *ulcers of the limbs of arterial origin* The last two medications not only cause vasodilatation of cutaneous blood vessels, but they are also of value in controlling the severe pain associated with a nutritional disturbance The production of a fever through the use of typhoid vaccine is likewise of benefit in the presence of ulceration, but it can only be used in young individuals (For further discussion see *Specific Therapy in Chronic Occlusive Arterial Vascular Disorders*, Chap IX)

Ganglionic Blocking Agents*

Etamon (Tetraethylammonium Chloride) This drug is an autonomic blocking agent affecting both parasympathetic and sympathetic ganglia Its therapeutic action in peripheral vascular disorders is dependent upon blockade of the paravertebral sympathetic ganglia as a result of which vasoconstrictor impulses arising in the vasomotor center are prevented from spreading over the postganglionic fibers to reach the peripheral blood vessels With subsequent release of vasomotor tonus, the arteries, arterioles, capillaries and arteriovenous shunts passively dilate However, as in the case of paravertebral sympathetic blocking with procaine various physical and chemical stimuli can still exert their pharmacologic action on the neuroeffector organ and the muscular coat of the blood vessels neither of which is influenced by the drug

That the vasodilating effect of Etamon is primarily on the cutaneous vessels in the limbs is supported by plethysmographic studies [7] With such means it has been shown that in the normal subject this drug causes a seven fold increase in blood flow in the hand and a four fold increase in the foot while only a negligible change occurs in the forearm and leg Unfortunately the circulatory alterations produced in patients with vascular disorders have not been determined However the effect on skin temperature has been investigated, and in individuals with arteriosclerosis obliterans and vasospastic diseases a rise has been noted but not as great as that with Priscoline [37]

Clinically Etamon has a limited application It has been found of some use in causalgia and in posttraumatic vasomotor disturbances but because it can only be administered parenterally, it has for the most part been replaced by such agents as Priscoline or Hydergine Another objection to the drug is that its intravenous administration is generally followed by a marked and at times alarming postural hypotension Generally the patient also experiences paresthesia in the lips, upper extremities, and toes In order to counteract this type of response, it is necessary to have him lie down for at least one half hour after Etamon is given

Hexamethonium Bromide Although this drug has received its greatest clinical trial in hypertension it also has been used in peripheral vascular disorders It is a ganglion blocking agent resembling Etamon but considered to be much more potent [15] With parenteral administration there is a definite increase in skin tem

*See Fig 80 p 458

This drug also acts on the sympathetic *neuroeffector* junction in the blood vessel wall to block its response to circulating adrenergic substances and adrenergic mediators involved in the transmission of vasoconstrictor impulses An increase in blood flow in the lower extremities of man occurs within an hour after intravenous administration [46]

Comprehensive clinical studies with Dibenzyline are meager since the drug has only recently become available It may be useful in counteracting to some extent the pain in causalgia[3] and the attacks of digital spasm in Raynaud s disease and Raynaud s syndrome It is also of value in controlling the hyperhidrosis associated with vasospastic states In the chronic stage of such organic vascular disorders as thromboangiitis obliterans and arteriosclerosis obliterans the routine and continuous use of Dibenzyline has no basis However if ulceration or gangrene exists then the drug may help facilitate healing

In all the above instances the oral route of administration can be utilized In the presence of marked spasm of collateral vessels initiated by occlusion of a main artery by an embolus the intravenous injection of the drug may help re establish the circulation However at present the preparation used for this purpose is not available commercially

There are several side effects associated with the administration of Dibenzyline which are manifestations of adrenergic blockade in other organs Even with oral use there may be dryness of the mouth nasal congestion and blurring of vision These generally become more marked with increased dosage of the drug and may be disagreeable enough to necessitate termination of the treatment Nausea head aches drowsiness and general malaise have also been reported Such symptoms usually tend to become less severe with continued administration In males there may be a reduction in the amount of seminal fluid With very large oral dosages or with intravenous injection a compensatory tachycardia and orthostatic hypotension may occur Where a fall in blood pressure already exists or is undesirable this drug should not be given Furthermore it is contraindicated in patients with compensated congestive heart disease since the tachycardia may precipitate frank failure

DRUGS HAVING A DIRECT VASODILATING EFFECT

There are a number of vasodilating drugs which exert their pharmacologic action directly on the muscular layer of the blood vessel As a result they are effective even after removal of sympathetic tonus through chemical blockade or sympathectomy

Histamine This drug or a histamine like substance is implicated in a number of physiologic processes such as local anoxia (p 468) local trauma prolonged exposure to cold and possibly exercise The pharmacologic action of histamine is characterized by a triple response elicited by its intracutaneous injection (Fig 2J p 8) First as a result of the direct action of the drug there is dilatation of cutaneous capillaries producing a uniform redness locally Second relaxation of arterioles takes place causing a more widespread mottled rubor Finally there is the production of a wheal due to increased capillary permeability That the latter state exists is supported by the findings of large quantities of protein in the edema

The therapeutic effectiveness of Priscoline is definitely limited by the fact that both the oral and the parenteral administration of this medication may be associated with severe side reactions. Within 15 or 20 minutes after the tablet is taken by mouth, the susceptible individual may experience chilliness with resulting "goose flesh," a sensation as though his hair were standing on end, and an uncomfortable warmth and prickly feeling in the face and neck. There may also be a sense of dizziness. Since the drug stimulates the secretion of hydrochloric acid, the patient may complain of pain in the epigastrium and a sensation of nausea, or he may even vomit. Generally, these gastrointestinal symptoms can be avoided if Priscoline is taken after meals. The drug should always be given orally with extreme caution if there is a history suggestive of peptic ulcer or gastritis.

Following intravenous injection the patient may experience a sense of weakness, marked flushing of the face, tingling and dizziness, tachycardia, and at times, arrhythmias. Because of the possible hypotensive effect there is some question as to whether it should be administered if coronary artery disease exists. It is of interest that there are some patients who can take large quantities of the drug both orally and parenterally without manifesting any of the above side effects.

Hydergine. This product is an equal mixture of three hydrogenated alkaloids of the ergotoxine group: dihydroergocornine, dihydroergocristine and dihydroergokryptine. By combining them more consistent results are obtained than from each individually. Besides the depressant effect on the vasomotor center already referred to, this drug has an adrenergic blocking action on the neuroeffector organ in the blood vessel wall. Both responses lead to vasodilatation of the peripheral arteries and arterioles. It has been shown that Hydergine inhibits or suppresses reflex vasoconstriction as from smoking cigarettes,[6] which is of importance in vascular disorders. It likewise eliminates the spontaneous volume changes in the extremities which are dependent upon alterations in vasomotor tonus.[13] Blood flow studies, using the venous occlusion plethysmograph, have revealed that the intravenous administration of Hydergine causes a significant increase in local circulation in the hand and foot but little change in the calf.[9] Finger blood flow is also augmented.[1]

Hydergine has been used in a number of different conditions, particularly Raynaud's disease, acrocyanosis, chilblains and frostbite. It appears to have some value in the treatment of ulceration and gangrene due to arteriosclerosis obliterans or thromboangiitis obliterans,[9] and it may be a useful adjuvant by parenteral administration when occlusion of a main artery by an embolus is associated with sudden spasm of collateral vessels. Finally, ulcers and dermatitis due to venous stasis appear to heal somewhat more rapidly when the drug is given.[39]

The side reactions of Hydergine are not marked. Occasional nausea or vomiting may be present and there may be a feeling of tiredness and headaches. Flushing of the face and neck and stuffiness of the nose may also be noted. Such responses are more likely to occur after intravenous than with intramuscular administration while rarely being noted with the use of sublingual tablets. The intravenous route is to be avoided because of the resulting depressant effect on blood pressure.

Dibenzyline (N-Phenoxyisopropyl-N-Benzyl-β-Chloroethylamine Hydrochloride).

forearm with only a slight augmentation in the leg[3] The response is probably due to local changes in the blood vessels In view of such a pharmacologic action the oral administration of nicotinic acid would appear to be of some value clinically in increasing blood flow in the hand and forearm particularly if the cause for the impaired circulation is vasospasm

Papaverine This drug, a member of the isoquinoline group of opium alkaloids, has a vasodilating effect on the peripheral vessels through its direct relaxing action on the muscle fibers of the media[30] When administered intra arterially it produces some increase in cutaneous temperature in the fingers and toes[7] The actual augmentation in the blood flow in the hand and foot observed with intravenous injection however is minimal[6] In the presence of spasm the dilating effect of the drug is enhanced If an involved artery can be exposed bathing it in papaverine may be successful in removing myogenic spasm when all other measures have failed (See Treatment of acute vascular spasm Chap XVII for further discussion of this point)

TOBACCO

Since it is generally accepted that tobacco smoking plays a role in the progress of thromboangiitis obliterans it appears necessary to discuss the pharmacologic action of this agent There is little question that in a small percentage of individuals it may have definite effects on the cardiovascular system These include pain resembling angina pectoris a rise in blood pressure tachycardia arrhythmias and electrocardiographic changes in the form of lowering or inversion of the T waves

In the case of the extremities skin temperature and plethysmographic studies[5, 6, 47] have revealed that tobacco smoking causes transient and reversible peripheral vasoconstriction The change is particularly marked in the fingers and toes where arteriovenous shunts are found in great abundance while little or no reduction in circulation occurs in the skin or muscle of the forearm and leg[5] The absence of change in muscle blood flow supports the belief that vasoconstriction by itself is not responsible for the deleterious effect of tobacco smoking on intermittent claudication noted clinically in patients with thromboangiitis obliterans The finding that the degree and duration of the decreased blood flow in the hands and feet in patients with occlusive arterial vascular disorders are no different from those observed in normal individuals is likewise in accord with such a view

The question arises as to what substances present in tobacco smoke are responsible for its pharmacologic action on the peripheral circulation The only one which has been given any physiologic significance is nicotine while the volatile materials arising from the combustion of cigarette paper evidently play a minor role in this regard[11] However it has been shown that smoke has an irritating effect on the respiratory tract producing peripheral vasoconstriction regardless of whether or not nicotine is present[17] In fact the associated deep breath alone will cause a similar type of response[34] It is possible, therefore that the reduced peripheral blood flow is due primarily to reflex vasoconstriction and secondarily to the pharmacologic action of absorbed nicotine

fluid and the rapid appearance of certain circulating dyes in the wheal which ordinarily pass slowly through the normal capillary wall

The formation of the wheal is independent of innervation by the sympathetic nervous system but is influenced by the rate of local blood flow and capillary blood pressure Because of this fact the response is used as a test in peripheral vascular diseases for the determination of the state of the cutaneous circulation (For technic of procedure, see *Histamine wheal test*, Chap II)

The intravenous administration of histamine produces both systemic and peripheral vascular responses which are transient, since the drug is rapidly destroyed by the kidney and other tissues Blood pressure is elevated[6] and cardiac output is augmented[20] Blood flow is increased in the hand during the time of injection and may remain so for the next 15–20 minutes[6] while other vascular beds show variable responses Such side effects as headaches and palpitation are common

The use of histamine by intra arterial injection and by ion transfer is of clinical value In both cases a definite increase in cutaneous blood flow occurs This is noted particularly in the hand and to a lesser extent in the forearm In the case of ion transfer, the change persists for an hour or more after the procedure is discontinued[1] Neither mode of administration produces side reactions

Acetylcholine and Mecholyl (Acetyl beta Methylcholine Chloride) Both systemic and peripheral vascular effects are produced by these substances when given subcutaneously intramuscularly, or intravenously Bradycardia and hypotension are consistently noted With intravenous injection there may be a slight flushing of the extremities while a more marked vasodilating effect is noted with the intra arterial route

The only method of administration of these drugs which has any clinical application is ion transfer When Mecholyl is given in this manner it causes a significant increase in blood flow in the forearm and foot and a lesser response in the leg[7] The changes appear during the period of application of current and persist for approximately an hour afterward They are due primarily to vasodilatation of cutaneous blood vessels while circulation in the muscle probably contributes little if any to the observed changes

Nitrites The main pharmacologic action of this group of drugs is a lessening of arterial tonus of the peripheral vascular system producing a fall in blood pressure as a result of the reduction in peripheral resistance With large doses because of the associated decrease in venous tonus there is a pooling of blood in the veins and as a consequence a decrease in venous return and cardiac output Since the systemic response to the parenteral administration of nitrites is so marked their use as therapeutic agents in peripheral vascular diseases is very limited However the local application of nitroglycerine in a base (Nitrol ointment) appears to have some value in producing an increase in cutaneous blood flow That absorption of the drug occurs after massaging it into the skin is supported by the frequent complaint of the production of a headache within several minutes after the onset of the treatment

Nicotinic Acid Aside from some flushing and prickling sensation in the face the effect of this drug on the peripheral vascular tree is limited to the vessels in the extremities A significant increase in blood flow is elicited in the hand and

marked vasoconstriction causes prolonged *compression* of the vasa vasorum and lymph spaces thus interfering *with the* nourishment of the vessel wall and eventually leading to degenerative changes.[7] Following thrombosis of an essential artery gangrene is inevitable.

EPINEPHRINE AND NOREPINEPHRINE

Since epinephrine and norepinephrine appear to play an important *role in the hormonal* regulation of peripheral *circulation* it is advisable to discuss their pharmacologic action in man. Blood flow studies using the venous occlusion plethysmographic method have revealed that the intravenous administration of small doses of epinephrine produces a significant but temporary increase in muscle circulation in the calf[19, 4] which with continuous infusion is followed by a much smaller but sustained augmentation.[8] The initial vasodilatation is not altered by sympathectomy from which it can be inferred that the change is due to the direct action of epinephrine on the vessels of the limb without the mediation of the sympathetic nervous system.[8] In contrast to the action of epinephrine that of norepinephrine on the muscle vessels is primarily vasoconstricting.[14]

Both epinephrine and norepinephrine produce a decrease in cutaneous circulation especially when administered intra-arterially.[43, 44] With intravenous injection epinephrine elicits a similar change but this is followed by an increase in blood flow after the infusion is stopped.[43, 44] Since the sympathectomized limb does not manifest the vasodilator response the possibility has been raised that the latter is due to depression of vasoconstrictor tone probably in the sympathetic ganglia.[10]

PROTEOLYTIC ENZYMES

Recently several proteolytic enzymes have been suggested as therapy in peripheral vascular disorders because of their ability to facilitate debridement of ulcers of arterial and venous origin. Varidase and Tryptar have received the most extensive clinical trial. Varidase consists of streptokinase and streptodornase (in the ratio of 3 or 4 1) which are enzymes excreted by streptococcal organisms into a culture medium. The potent factors are separated from bacteria purified and filtered. Streptokinase apparently catalyzes the transformation of plasma plasminogen to plasmin an active fibrinolysin in human plasma. As a consequence fibrin is split into polypeptides thus resulting in dissolution of blood clots and fibrinous exudates. For this reaction to occur the presence of serum and an alkaline medium is essential. Streptodornase liquifies desoxyribonucleoprotein and desoxyribonucleic acid main constituents in nuclei and so causes a marked reduction in the viscosity of purulent exudates. It does not act upon nuclei in living cells[42, 4] nor does it have any fibrinolytic activity.

Tryptar a crystalline trypsin derived from mammalian pancreas produces selective digestion of nonviable cells and tissues into peptides and amino acids. It acts on the slimy and viscid coating of desoxyribonucleoprotein of the purulent

A hypersensitivity to tobacco has been suggested as an explanation of the changes produced in thromboangiitis obliterans when smoking is continued Such a view is based on the finding of an allergic skin reaction to nicotine free tobacco extract in a high percentage of patients with this disorder[20-24] On the other hand, changes in cutaneous temperature of the toes, blood pressure, and pulse rate produced by smoking have not been found to be consistently different in persons who show skin sensitivity to tobacco than in those who do not[31] The fact that smoking has the same pharmacologic effect on women as on men is also evidence that hypersensitivity of tobacco is not an etiologic agent in thromboangiitis obliterans for in this disease, females are affected only rarely

The form in which tobacco is used determines the amount of nicotine available for absorption[3] The greatest quantity per unit of weight is obtained from cigars and pipes and the least from cigarettes, probably because of the more nearly complete combustion of nicotine associated with the smoking of the latter Tobacco chewing also causes a greater absorption of nicotine than does cigarette smoking

It would appear, therefore, that pharmacologic studies on tobacco smoking although demonstrating unequivocally that vasoconstriction occurs in the peripheral vessels are of little value in elucidating the basis for the unquestioned harmful and progressive effects of this habit in thromboangiitis obliterans Some other factor, at present unidentified, must be implicated In the case of vasospastic disorders it is understandable why smoking, by causing constriction of vessels already highly sensitive to all types of noxious stimuli, is contraindicated Furthermore, in conditions in which the greatest possible cutaneous blood flow is desired the vasoconstricting effect of smoking on skin vessels should likewise be eliminated

ERGOT AND ITS DERIVATIVES

Since ergot preparations have extensive use in obstetric practice and in the treatment of migraine and pruritis associated with jaundice and since these substances may on occasion produce vascular difficulties it is necessary to present their pharmacologic action Most of the experimental work has been done using ergotamine tartrate This drug produces a fall in systolic blood pressure frequently preceded by an initial rise and a slowing of the heart At the same time there is a definite decrease in blood flow in the hand[4]

In the case of susceptible individuals or in the presence of an overdose ergot preparations may cause widespread changes in the peripheral vascular tree in some instances leading to nutritional disturbances One of the early findings is the disappearance of peripheral pulses Later pain (particularly muscular cramping) peripheral paresthesia a decreased cutaneous temperature and cyanotic mottling may appear In some instances actual gangrene of a digit or digits will occur and even death An infrequent sequel is Raynaud's phenomenon

The basis for the pathologic changes in ergotism is first severe vascular spasm which can not be removed by sympathetic denervation and subsequently thrombosis, due to stasis and injury of the intima The involvement is widespread in medium and small sized arteries arterioles and capillaries It is possible that the

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exudate and then attacks dead tissue in the lesion, causing the exudate to become thin and serous[30, 38] Thus pus and debris are eliminated and the formation of healthy granulation tissue is facilitated

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APPENDIX

SOURCES OF PROPRIETARY DRUGS, INSTRUMENTS, AND SURGICAL OR LABORATORY SUPPLIES

It has been felt advisable to make available for the convenience of the reader the names of the manufacturers of the various proprietary medications instruments and surgical or laboratory supplies mentioned in the text This does not necessarily imply endorsement of the listed products or criticism of those not included

Source of Drugs

1 Asterol dihydrochloride (2-dimethylamino-6-[β-diethylamino ethoxy] benzothiazole dihydrochloride)
Hoffmann La Roche Inc
2 Aureomycin (chlortetracycline hydrochloride)
Lederle Laboratories
3 Benadryl (diphenhydramine hydrochloride)
Parke Davis & Co
4 Biohepulin (extract of livers from pregnant cattle)
International Biochemical Corp
5 Chloresium ointment (chlorophyll ointment)
Rystan Co
6 Chloromycetin (chloramphenicol)
Parke Davis & Co
7 Dalisol (combination of copper sulfate and zinc sulfate)
Dome Chemicals Inc
8 Daxalan ointment (crude coal tar zinc oxide starch and mineral oil)
Dome Chemicals Inc
9 Depo-Heparin Sodium
Upjohn Co
10 Depropanex (deproteinated pancreatic extract)
Sharp & Dohme
11 Desenex (zinc undecylenate undecylenic acid and talcum)
Wallace & Tiernan
12 Dibenamine (dibenzyl β-chloroethylamine)
Smith Kline & French Laboratories
13 Dibenzyline (N phenoxyisopropyl N benzyl β-chloroethylamine hydrochloride)
Smith Kline & French Laboratories
14 Etamon (tetraethylammonium chloride)
Parke Davis & Co

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3 Dome boot
Dome Chemicals Inc
4 Intermittent venous occlusion machine
Burdick Corp Chicago
U M A Inc New York N Y
5 Oscillometer
Boulitte Co Rheinbeck, N Y
U M A Inc New York, N Y
Taylor Instrument Co Syracuse N Y
6 Skin temperature thermocouple
U M A Inc New York, N Y

15 Hedulin (2 phenyl 1, 3 indandione)
Walker Laboratories Inc
16 Heparin in Pitkin menstruum
Wm R Warner & Co
17 Hydergine (equiproportional mixture of dihydroergocornine methanesulfonate dihydroergocristine methanesulfonate and dihydroergokryptine methanesulfonate)
Sandoz Pharmaceuticals
18 Lyocyte powder (red blood cell powder)
Sharp & Dohme
19 Mecholyl (acetyl β methylcholine chloride)
Merck & Co
20 Metycaine (piperocaine hydrochloride)
Eli Lilly & Co
21 Nitrol ointment (2% nitroglycerine in ointment base)
Kremers Urban Co
22 Padutin (pancreatic extract)
Winthrop Stearns Inc
23 Parenzyme (trypsin in sesame oil)
National Drug Co
24 Pontocaine (tetracaine hydrochloride)
Winthrop Stearns Inc
25 Priscoline (2 benzylimidazoline hydrochloride)
Ciba Pharmaceutical Products Inc
26 Sopronol (propionate caprylate [fatty acid compound])
Wyeth Laboratories
27 Sulfamylon with streptomycin (mafenide [4 amino ethyl benzenesulfonamide hydrochloride] with streptomycin)
Winthrop Stearns Inc
28 Thiopental (sodium pentothal)
Abbott Laboratories
29 Timofax (10% undecylenic acid)
Burroughs Wellcome & Co
30 Tromexan (bis 3 3 [4 oxycoumarinyl ethyl acetate])
Geigy Co Inc
31 Tryptar (purified crystalline trypsin)
Armour Laboratories
32 Varidase (streptokinase and streptodornase)
Lederle Laboratories
33 Vioform (iodochlorhydroxyquin [containing 41% iodine])
Ciba Pharmaceutical Products Inc

Source of Instruments and Specific Surgical or Laboratory Supplies

1 Bandages 4 inch elastic bandage Ace # 8
Becton Dickinson & Co
Pure gum rubber bandage
Weber & Judd Rochester Minn
Webril cotton roll
Curity
2 Compression legging (Aero pulse Legging)
Surgical Research Corp Rochester N Y

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Set in Linotype Electra
Format by Katharine Sitterly
Manufactured by The Haddon Craftsmen Inc
Published by HARPER & BROTHERS New York